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A STUDY OF A CASE OF CERVICAL GLIOMA.

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(With Plates XIX-XXI.)

THE following case of a glioma involving the cervical portion of the spinal cord is described somewhat fully since, apart from its rarity, the clinical course presented certain very definite difficulties in diagnosis and, further, since the structure of the neoplasm is of considerable interest.

W. D., male, aged 31, a motor mechanic, first consulted Professor Edwin Bramwell on October 20, 1927. The patient had been well until a couple of months previously: he then began to have some pain about the left shoulder, which he was inclined to attribute to a twist while winding up the engine of his car. The pain had gradually got better, but the upper part of his left arm had slowly become weaker; a little later he noticed that the right arm was becoming affected; the weakness in the arms increased progressively. The deltoids, the biceps and infraspinati muscles on both sides showed pronounced weakness with accompanying wasting. The upper parts of both trapezii, the sternomastoids and the pectoral muscles were acting well, but on the left side the action of the lower part of the trapezius was defective. The movements of the hands and of the wrists were unimpaired. On the thumbs, index fingers and outer sides of both fore-arms there was some sensory loss to pain though not to touch. The pupils and palpebral fissures were equal. No deformity, tenderness, or limitation of movement of the cervical spine was present. There was no weakness in the lower limbs; the knee-jerks were hyperactive and equal; the plantar reflexes were flexor in type. The tentative diagnosis made at this time was that of a localized lesion, most probably intermedullary, at the level of the fourth and fifth cervical segments.

On October 28, 1927, the patient was admitted to Professor Bramwell's ward at the Royal Infirmary, Edinburgh. Some days previously he had

wakened in the middle of the night with pain in the back of the neck, but this disappeared after he made some movements. The weakness of the arms had become progressively worse till, when examined in hospital, the patient was quite unable to lift the left arm and, with the right arm, movement was possible only below the elbow. On both sides, but to a greater degree on the left side, the deltoid, biceps, brachio-radialias, infraspinatus and supraspinatus were markedly atrophied. The dynamometer readings were: left hand, 90; right hand, 110. There was no inco-ordination or intention tremor and there were no fibrillary tremors of muscles. The wrist and triceps jerks were active and equal on the two sides, but the biceps-jerk was only just perceptible on the right side, and absent on the left. The abdominal reflexes were active. The jaw-jerk was unusually active. Knee and ankle jerks were hyperactive, but there was no clonus. Plantar responses were flexor. Tenderness was elicited on pressure over the fourth cervical spine, but, in contrast to the sensory disturbance present eight days previously, no loss to pain could now be detected in the arms.

On November 1, 1927, the cerebrospinal fluid was examined for Wassermann's reaction and gave a negative result: the globulin was slightly increased in amount; cells were 2 per c.mm.; and the colloidal gold curve was 0012331100. X-ray photographs of the cervical region showed no abnormal appearances.

The patient remained in hospital until January 14, 1928. During the first part of this period pain was occasionally present in the middle line at the level of the fifth and sixth cervical spines, but was controlled by pyramidon, 5 gr. Nearer the end of his stay in hospital, however, the pain was more constantly present and kept him awake at night. Treatment at first consisted of potassium iodide, 25 gr. t.i.d., and mercurial inunction: later, hypodermic injections of strychnine in increasing and decreasing doses were substituted. Some time after the course of injections had commenced the increased tendon reflexes in both legs became more exaggerated. Throughout the patient's stay in hospital the jaw-jerk was always elicited very easily. Before his discharge no additional muscles had become noticeably atrophied, and the weakness in those already affected had become only slightly more marked.

On February 14, 1928, the patient reported. He had suffered a considerable amount of pain in the neck, varying in intensity. The muscular weakness had gradually become more pronounced. Dynamometer readings were: left hand, 60; right hand, 85. There was now a definite extensor response on the left side, but the right plantar reflex was still flexor. The patient had never experienced any difficulty in walking.

On March 10, 1928, the patient again reported. In the interval the neck had become somewhat stiff, but the pain had not been so severe. The weakness in the hands had progressed and both arms were now practically powerless. Dynamometer readings were: left hand, 35; right hand, 60. When walking he experienced a stiffness of the legs and at times he tended to stagger. The plantar reflexes were the same as on the previous occasion.

On April 11, 1928, the patient was readmitted to hospital. The weakness in the left hand had now advanced until it was absolutely powerless. Dynamometer readings were: left hand, 0; right hand, 50. Examination revealed over the limbs and trunk, from the fifth cervical distribution downwards, a general impairment of sensation to pain and temperature, but not to touch. Cerebrospinal fluid was withdrawn simultaneously by cistern and lumbar punctures. The fluid from the lumbar route was xanthochromic and the pressure did not vary either on coughing or on compression of the jugular veins: that from the cisternal route was clear and, on both tests, showed a sharp rise in pressure. Examination of the two fluids showed:—

Lumbar.— Cells = 17 per c.mm. Globulin markedly increased.

Cisternal.—Cells = 2 per c.mm. Globulin—a trace.

Following these punctures the patient experienced considerable pain in the neck and shoulders on both sides, and rapidly became paraplegic with incontinence of bladder and bowel.

The respective contents of the cerebrospinal fluid from the two sources showed that a blockage existed within the spinal theca, somewhere between the cisternal and lumbar regions; from the other clinical data, the level of the lesion was undoubtedly in the neighbourhood of the fifth, sixth and seventh cervical segments.

Professor Wilkie was asked to see the patient with a view to operation, and it was decided to perform an exploratory laminectomy.

On April 19, 1928, the fourth to the seventh cervical spines and laminæ were removed and the underlying dura mater exposed. The membrane looked and felt tense; the normal space between it and the posterior arch was obliterated, but the bony surfaces were not eroded. The third and seventh vertebral arches were then removed. The dura was incised in the mid-line about the level of the fourth cervical vertebra. There was a sudden gush of cerebro-spinal fluid under tension, but it was clear and not pigmented. The incision in the dura was extended to the extremities of the wound and, so far as could be seen, the vertebral canal was filled completely by a growth. The growth was examined above, below, and at the sides, but no point of separation of tumour from cord was found. The tumour consisted of a fusiform expansion of the substance of the cord. Removal therefore was out of the question, and 10 mg. of radium were laid in tubes on the surface (one tube of 5 mg. and five tubes of 1 mg.).

A few hours after the operation the patient died of shock.

Autopsy.—At autopsy the brain, spinal cord and spinal meninges were removed in one piece. The fusiform expansion of the substance of the cord was found to extend from about the third cervical to the first thoracic segment. Laterally, and also posteriorly, between the levels at which the nerve roots entered the cord, nodular swellings were present (fig. 1). The whole tumour was surrounded by the pia-arachnoid membranes and at no place was it adherent to the dura mater. Away from the swelling, no abnormality of the spinal cord was observed.

After fixing in formol-ammonium-bromide for a few days, the cord was examined by making transverse incisions at various levels.

Two separate and small hæmorrhages were found, one on each side in the antero-lateral portions of the cord and extending from the sixth cervical to the first thoracic segments. The maximum area of that on the right side occurred in the seventh cervical segment. The hæmorrhage on the left side was smaller in transverse extent than was that on the right side.

In sections taken transversely through the centre of the fusiform swelling, no differentiation into grey and white matter was seen. To the naked eye the medulla was not involved by the neoplasm, but subsequent microsoopic examination showed that it had extended for some distance into this region.

Microscopic examination.—(1) A portion comprising the whole transverse diameter was taken from the centre of the fusiform swelling and was placed for twenty hours in Helly's modification of Zenker's fixative and thereafter carried through the routine procedure for paraffin sections. These were stained by Meyer's acid hæmatin and eosin.

(2) Frozen sections of the tissue removed from various levels were impregnated by Cajal's gold chloride sublimate method and by various silver methods.

Sections cut in paraffin and stained by hæmatin and eosin demonstrated that in the centre of the fusiform swelling the entire internal structure of the cord had disappeared, the whole tissue being a mass of protoplasm very rich in nuclei. As compared with the nuclei of the peripheral protoplasm, those in the central parts were small, deeply staining, and were losing their structure (pyknotic changes).

The nuclei of the peripherally situated protoplasm varied in size: the great majority of them were round or oval, large, and rich in chromatin. Some of the oval nuclei were of great size and contained a large amount of deeply staining chromatin.

In certain places the nuclei were grouped together, giving the appearance of a multi-nucleated or polymorpho-nucleated giant cell. In some instances, these groups of nuclei were of the extremely large type (fig. 2).

The structure of the neoplasm, therefore, as demonstrated in paraffin sections, was typical of the "giant-celled glioma of Stroebe."

For the most part, the blood-vessels in the neoplasm were not numerous and their walls were not thickened. In a few instances the smaller vessels contained hyaline thrombi.

Numerous small rounded or oval masses of calcareous material were present in those portions in which the nuclei were undergoing pyknotic changes; the deposition had occurred in the form of small spherular bodies, and hence the whole mass had a crenated outline. In certain instances the small spherules were discrete and scattered over a rather larger area than that occupied by the aggregations. In other instances the deposition had occurred in the perivascular sheaths of small blood-vessels (fig. 3).

Transverse sections taken from the centre of the fusiform swelling (cervical

FIG. 1.—Illustrates the fusiform expansion of the cord due to the glioma.

To illustrate paper by James K. Slater and F. E. Reynolds.

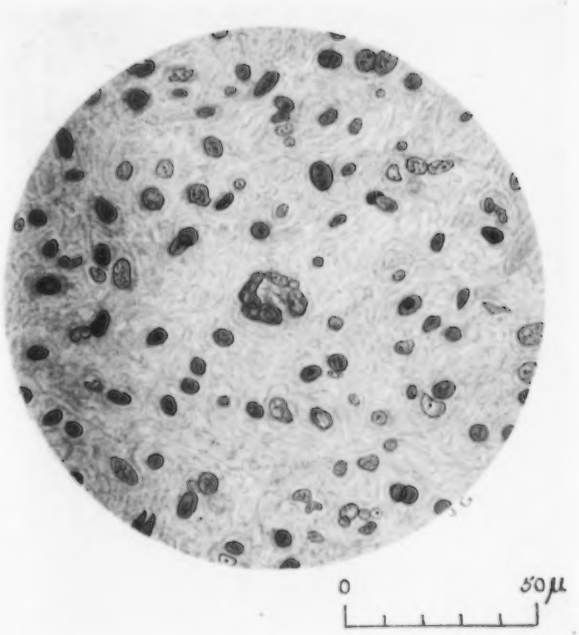

FIG. 2.—Paraffin section stained by hæmatoxylin and eosin. The nuclei, large, round or oval, are rich in chromatin. In the centre of the field they are grouped together, giving the appearance of a multinucleated or polymorphonucleated giant cell.

PLATE XIX.

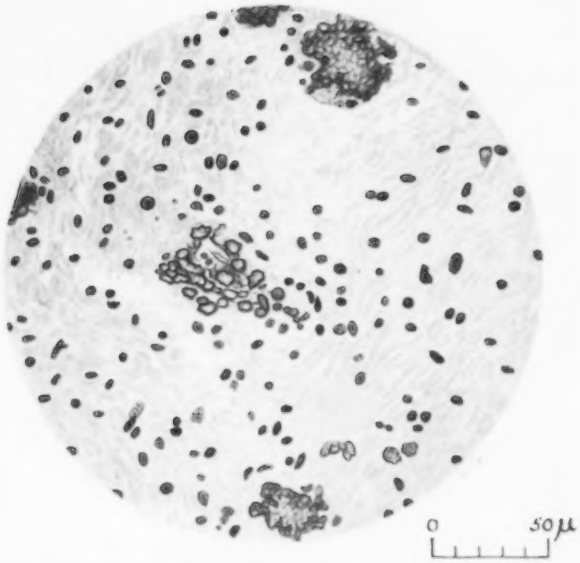

FIG. 3.—Paraffin section stained by hæmatoxylin and eosin. Small globular masses of calcareous material have been deposited in an area of the glioma undergoing necrotic changes. In the centre of the field the deposition is seen to have occurred around a small blood-vessel.

FIG. 4.—Frozen section treated by Cajal's gold chloride sublimate method. Two of the pre-existing astrocytes involved by the glioma are in process of disintegration.

To illustrate paper by James K. Slater and F. E. Reynolds.

segment 6), treated by various silver impregnation methods and by Cajal's gold method, showed that for the most part the neuroglial septa had disappeared, small portions only remaining: no trace of the central canal was seen. A certain number of astrocytes in various stages of disintegration were still present; their bodies and processes were swollen and the latter were to a greater or lesser extent fragmented (clasmatodendrosis, fig. 4).

The structure of the neoplasm was that of a syncytium: numerous large nuclei, varying greatly in size, were embedded in a protoplasmic matrix in which were no cell boundaries (fig. 5).

Transverse sections taken through the lower part of the neoplasm (level of cervical 8 and thoracic 1) showed that the neoplastic growth in the cord was confined to the posterior columns: the membrana superficialis and the septa were intact, but the pia-arachnoid meshes dorsal to the posterior portion of the cord were distended and filled by the neoplasm. In these situations the structure of the neoplasm was of the same syncytial character as was found elsewhere. Serial sections cut in paraffin showed that the neoplasm had reached the pia-arachnoid spaces by infiltrating along the posterior roots.

A cyst some 2 mm. in diameter, due to liquefactive necrosis of neoplastic tissue, was present in one of the posterior columns immediately behind the grey commissure. Its wall was composed of the pre-existing interstitial elements of the cord in which were islands of more or less necrotic neoplastic tissue: it contained fluid with a certain number of fragmented fibres and granular corpuscles.

Paraffin sections showed that certain portions of the tissue around the cyst were very vascular, numerous well-formed blood-vessels being present, and in this area a segment of the wall consisted of very recently proliferated capillaries.

The astrocytes of the grey matter, but particularly those of its antero-lateral portion on both sides, were undergoing very active amitotic proliferation: they were numerous, large, and deeply impregnated by gold: some of them contained two nuclei and many of them were closely approximated in pairs.

Longitudinal sections were made from a portion 2·5 cm. long, comprising the upper part of the spinal cord and lower part of the medulla. These sections showed that strands of the neoplasm had infiltrated upwards: at the lower levels some of the strands were of considerable size. In the medulla they were numerous but narrow, passing between and parallel to the nerve fibres.

Sections prepared by Gross-Bielschowsky's method demonstrated that where the neoplastic tissue was large in amount the majority of the nerve fibres had disappeared. Those which had persisted were greatly atrophied and some of them showed fragmentation (fig. 6). Nodular swelling and the other forms of degeneration of nerve fibres found in experimental lesions (Cajal and others) were not observed.

Longitudinal sections of the lower part of the neoplasm and of the adjacent cord presented a similar picture to the above, the neoplasm extending in the form of wider and narrower strands. Proliferation of astrocytes was again marked, especially in the grey matter which had not been involved by the new growth.

From the above it will be observed that in no part of the neoplasm was there any differentiation of the syncytium into cell elements resembling spongioblasts or astrocytes.

Commentary.

(1) *Pathology.*—It is commonly stated that a glioma rarely, if ever, spreads from the substance of the brain or cord into the pia-arachnoid spaces, whereas an ependymoma of the brain-stem or cord frequently does so. It might be maintained, therefore, that the neoplasm in this case had arisen from the ependyma and not from the neuroglia. Such a differentiation is of no moment, however, since genetically both the ependyma and neuroglia are identical. At most, the so-called "ependymoma" can be considered only as a type of glioma.

The preparations treated by the gold and silver methods demonstrate the neoplasm to be a syncytial glioma throughout The type of neuroglia of which the neoplasm is composed has its counterpart in the earliest form of developing neuroglia present in the neural tube, namely, the syncytium described first by His. The only histological difference between the elements of the neoplasm and of the normal syncytium of the neural tube in its earliest stages is in the increased number and varied size of the neoplastic nuclei and in their large chromatin content.

Had the patient survived longer, it is conceivable that the neoplastic syncytium would have become differentiated into individual neuroglial cell elements, having as their prototypes normal spongioblasts or even astrocytes. It seems probable to us, however, that such differentiation would not have occurred, since it is justifiable to presume that the neoplasm would have continued to extend, but that the relative phases present at the time of death would have been maintained, namely, a progressive zone of newly-formed living neoplasm surrounding a core in which necrotic changes were simultaneously advancing.

In the present case the necrobiotic changes in the central portions of the neoplasm might be explained by the increasing pressure of the growth against the dura mater and surrounding bony canal gradually diminishing the vascular supply and so leading to inadequate nourishment. In general, however, necrosis occurring in neoplasms can be explained only to a certain extent by insufficient blood-supply; some other factor, at present undefined, must come into play.

So far as we are aware, no neoplasm having a structure typical of the "large-celled glioma of Stroebe" has been investigated hitherto

by gold and silver impregnation methods. In the present case the latter methods have shown that the structure associated with the "large-celled glioma" is that of a syncytium.

After we had demonstrated, in the present case, the identity of the large-celled glioma as shown in paraffin sections with that of a syncytium, we examined two other cases of Stroebe's neoplasm, paraffin sections of which were in our collection. From these three cases we are convinced that the syncytial character of the neoplastic neuroglia is the true interpretation of the type associated with the term "large-celled glioma."

The deposition of the calcareous material in the present case requires consideration. Deposition of calcareous salts in dead material is a frequent occurrence and, speaking generally, it is quite commonly met with in the portions of neoplasms which have undergone necrosis. Although necrosis occurs almost invariably in parts of gliomata, it is exceedingly rare to find calcareous deposition taking place within it. Why this is so is difficult to explain; calcareous deposition in necrotic tissue is intimately related to fatty material deposited in the process of disintegration. In areas of necrosis in the central nervous tissues, lipoids and other bodies of a fatty nature are found in large amounts, and it might be expected therefore that the brain and cord would be a frequent site of calcareous deposition in conditions in which disintegration of their tissue takes place. Although the large amount of fatty bodies resulting from the disintegration of the elements of the cord may explain the deposition of the lime salts in the present case, it seems to us to shed no light as to why similar deposition does not occur frequently in gliomata.

The last point which we propose to discuss in the pathology of this case is the proliferation of the astrocytes adjacent to the neoplasm.

It has been noted that both at the upper and at the lower ends, where the neoplasm was not occupying the whole area of the cord but was extending in the form of narrow infiltrating processes, the astrocytes in the neighbourhood were undergoing active proliferative changes.

In the majority of those gliomata in which the neoplastic cells become differentiated to the degree of forming astrocytes, it is this change at or near the growing portions which gives rise to difficulty in deciding, firstly, whether the proliferating astrocytes are neoplastic or pre-existing, belonging to the "normal" tissue of the cord, and secondly, whether the change is one affecting the pre-existing astrocytes, causing them to become neoplastic under the influence, as it were, of the neighbouring new growth.

In the present case there can be no possible confusion between the neoplastic tissue and that pre-existing, since the structure of the former is syncytial throughout its whole extent. Moreover, the complete differentiation and histological perfection of the proliferating astrocytes in this case make it certain that the changes are those of proliferation and not a metamorphosis into a neoplastic state.

Further, proliferative changes in the connective tissue in the neighbourhood of a neoplasm occur in many infiltrating new growths other than gliomata. The question as to whether the proliferative changes in the neighbouring stroma are to be interpreted as a neoplastic change does not arise in these cases, since the tumour cells and the stroma cells are of an entirely different structural character, e.g., epithelial and connective tissue.

Various interpretations have been given to the significance of the proliferative changes in the stroma. One of the commonest put forward is that they are an expression of a defensive mechanism; in other words, that it is an attempt on the part of the body to form a barrier to the invasion of the neoplasm. We are not prepared to accept this as the true meaning of the reaction.

That wherever damage and destruction of tissue occurs, proliferative changes take place in those cells which have retained the potentiality to divide, is a law of general application. This is seen, for example, in the case of a wound in any part of the body and in inflammatory processes wherever they occur. It is outside our present purpose to discuss the nature of the stimulus to this reaction, but we suggest that probably it is associated with the products of autolysis of the dying tissue elements and that the reaction is the result of phylogenetic development, since it is the fundamental process underlying healing and repair.

In the case of an invading neoplasm tissue is destroyed and, according to the general law enunciated above, the neighbouring cells, capable of proliferating, will pass into an active vegetative phase and begin to divide. Moreover, if the stimulus to proliferate be in whole or in part what we have suggested, the lytic products may be reinforced by products derived from the metabolism of the neoplastic cells. It is known that these differ from the products of the "normal" cells and, being "abnormal," they may act on the neighbouring cells, stimulating them to reproduce just as do the products of lysis.

(2) *Clinical course.*—The case presents several features of clinical interest. When first seen the distribution of the progressive wasting

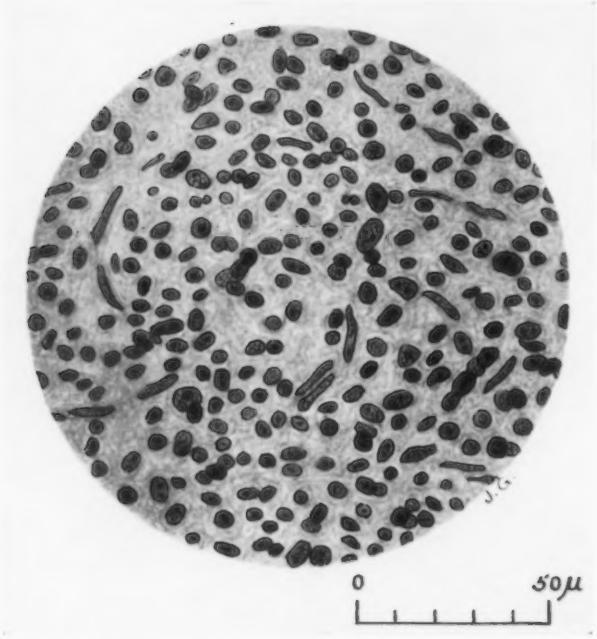

FIG. 5.—Frozen section, treated by Hortega's silver carbonate method, demonstrates the syncytial character of the glioma. (The elongated nuclei are those of the endothelial cells of the blood-vessels.)

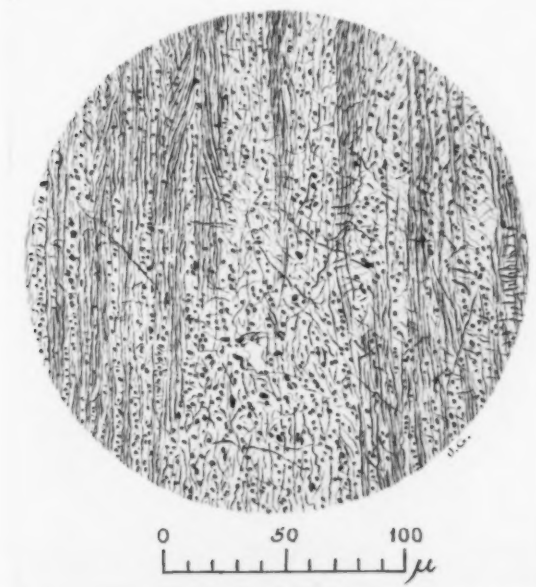

FIG. 6.—Longitudinal section from the upper part of the neoplasm, treated by Gross-Bielschowsky's method, shows the tumour extending in the form of infiltrating strands. The nerve-fibres are atrophying and disappearing.

To illustrate paper by James K. Slater and F. E. Reynolds.

and its symmetry, the pain which had been complained of about the spine of the left scapula, and the sensory impairment along the radial aspect of the upper limbs, pointed to a gross lesion at the level of the fourth, fifth, and sixth cervical segments of the spinal cord. The preponderance of the motor symptoms and the absence of evidence of interference with conduction in the spinal cord suggested that the lesion was situated anteriorly, although it was doubtful whether it lay in the substance or on the surface of the cord. Again, the X-ray examination showed no evidence of disease of the bone, while the negative result of Wassermann's reaction and the inefficacy of treatment with iodide and mercury appeared to justify the exclusion of a syphilitic lesion. Further, the examination of the cerebro-spinal fluid at this period afforded no positive diagnostic evidence. The facts that after the patient's admission to hospital no sensory disturbances were detected, that the jaw-jerk was unusually active, and that the pain complained of had never been an obtrusive symptom, raised the question whether the case might be one of amyotrophic lateral sclerosis. The muscular wasting, however, was strikingly symmetrical and conformed with a nerve-root distribution; moreover, there were no fibrillary tremors.

At a later date the results of combined cistern and lumbar punctures, together with the onset of sensory disturbance with a spinal distribution corresponding to a particular level, afforded definite proof of the presence of a gross lesion not only interrupting the circulation of the cerebro-spinal fluid but also involving the cord in the mid-cervical region. The lesion was undoubtedly a neoplasm, but whether situated in the substance or on the surface of the cord was still doubtful, and this was only determined at the operation.

As demonstrated at autopsy, the relationships of the neoplasm showed that the pain complained of must have been due to pressure by the tumour upon the fourth and fifth posterior cervical roots. Again, the paraplegia which developed so suddenly after the cistern and lumbar punctures was caused most probably by disturbance of pressure followed by hæmorrhage. It may be that the cerebro-spinal fluid above and below the tumour was exerting a protective influence by distending the theca, and that its removal resulted in rupture of two or more diseased blood-vessels.

(3) *Gliomata of the cord in general.*—The great majority of cases published under the title of tumours of the cord refer to neoplasms arising, not from the cord but in association with its membranes.

The only neoplasms which can arise from elements of the spinal

cord are: (*a*) gliomata (including ependymomata); and (*b*) those in which the specific cells have as their prototype the nervous parenchyma (neurocytomata).

In a series of 187 cases collected by Ewing ("Neoplastic Diseases," 3rd edition, Phila., 1928), of neoplasms occurring within the bony canal of the spine, only 45 (24 per cent.) were actually neoplasms of the cord.

Statistics, quoted by Elsberg ("Tumours of the Spinal Cord," London, 1925) from different sources and collected by various authors, give the number of intramedullary as compared with extramedullary neoplasms of the cord as between 20 and 28 per cent. In his own cases, out of 100, only 14 were found to be intramedullary. A further analysis of these 14 cases showed that 8 (57 per cent.) occurred in the cervical and 6 (43 per cent.) in the thoracic portion. But it should be remembered that Elsberg's figures are taken from the statistics of a surgical clinique.

Schlesinger's statistics ("Beiträge zur Klinik der Rückenmarks- und Wirbeltumoren," Jena, 1898) show that whereas in the dorsal region meningeal neoplasms are four times as frequent as medullary growths, in the enlargements the latter tend to predominate.

Many authorities look upon the neuroglial hyperplasia, which is the essential change in syringomyelia, as being of the nature of a neoplasm (glioma) extending for a shorter or longer distance in the cord. Personally, we do not agree with this view. It seems to us that the essential difference between hyperplasia of the neuroglia (gliosis), such as occurs in syringomyelia and neoplastic growth (glioma), is that in the former, although reproduction of the neuroglial elements occurs, the growth is restrained, whereas in neoplastic proliferation the growth is uncontrolled.

Summary.

(1) The present study is of a glioma extending from the third cervical to the first thoracic segment of the cord. It had extended along certain of the posterior nerve-roots and thence had invaded the neighbouring pia-arachnoid spaces, producing nodular swellings.

(2) The patient was observed clinically for a period of six months, and certain difficulties in diagnosis arose; these are discussed.

(3) The neoplasm consisted of a syncytium; nowhere had differentiation into individual cell elements taken place.

(4) Gold and silver impregnation methods demonstrated that in the present case the structure associated with "the large-called glioma of Stroebe" is that of syncytium.

(5) Proliferation of the pre-existing astrocytes of the cord had occurred in the neighbourhood of the syncytial neoplasm. The significance and cause of this phenomenon is discussed.

In conclusion, we wish to express our thanks to Professor Bramwell for supplying us with the clinical records and for permission to publish the present case; further, we wish to acknowledge the valuable help and criticism we have received from him in preparing the case for publication. We wish also to acknowledge the assistance given to us by the Medical Research Council by the aid of a grant towards the expenses of the investigation, and by the Carnegie Trust for financial assistance in publishing the illustrations.

A STUDY OF THE PATHOLOGY OF A CASE OF GLIOMA CEREBRI.

BY F. E. REYNOLDS, M.B.
(Superintendent of the Laboratory of the Scottish Asylums Board.)

(With Plates XXII-XXIV.)

THE pathology of the present case of a glioma cerebri follows in natural sequence the case published by James K. Slater and F. E. Reynolds in the present volume of *Brain* ("A Study of a Case of Cervical Glioma," p. 425). Moreover, the investigation has helped to confirm our views as to the unscientific basis of certain classifications of gliomata which have been advanced in recent years, views which have been impressed upon us by the investigation of a considerable number of these neoplasms carried out in the Laboratory of the Scottish Asylums Board.

J. D., male, aged 46, a mining inspector, was admitted to Professor Ritchie's ward in the Royal Infirmary of Edinburgh, on February 3, 1928, complaining of severe frontal headache, drowsiness, and vomiting. The patient had enjoyed excellent health up to a week before admission to hospital, when the symptoms had commenced suddenly.

On examination, the patient was apathetic, but he was not aphasic; papillœdema was marked in both eyes; there was no muscular weakness or inco-ordination; the reflexes were present and equal. Wassermann's reaction on the blood gave a negative result.

Some days later, the patient developed a left-sided paresis. He gradually passed into coma and, a hypostatic pneumonia supervening, died on February 23, 1928, some four weeks after onset of symptoms.

Autopsy.—The cerebral convolutions on both sides were found to be markedly flattened.

After removing the brain, a medial sagittal section showed the body and the knee of the corpus callosum to be involved by a neoplasm, but the splenium had not been invaded. The portion of the neoplasm situated in the corpus callosum was pinkish in colour with dark areas of necrosis (Plate XXII, fig. 1).

Sagittal sections were made through each hemisphere. On the *right* side, the neoplasm, which was rather paler in colour than the cerebral tissue, extended diffusely both in an antero-posterior and in a lateral direction,

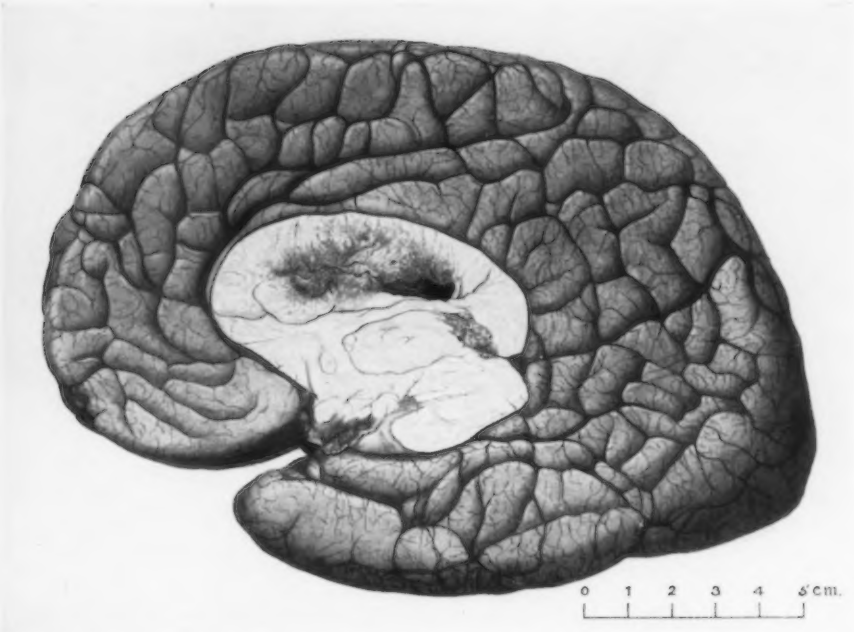

FIG. 1.—Medial sagittal section showing involvement of the body and knee of the corpus callosum by the glioma.

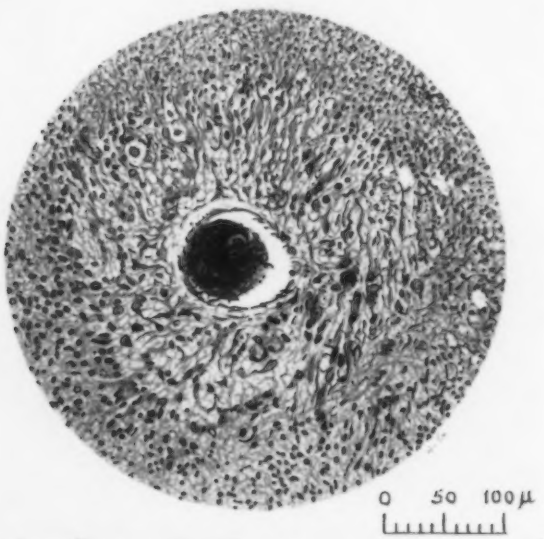

FIG. 2.—From a necrosing portion of the glioma. The neoplastic tissue immediately around the central blood-vessel is still living, whereas that more distant is necrosed. The phenomenon is that of the so-called "pseudo-rosette." Frozen section treated by Hortega's silver carbonate method.

To illustrate paper by F. E. Reynolds.

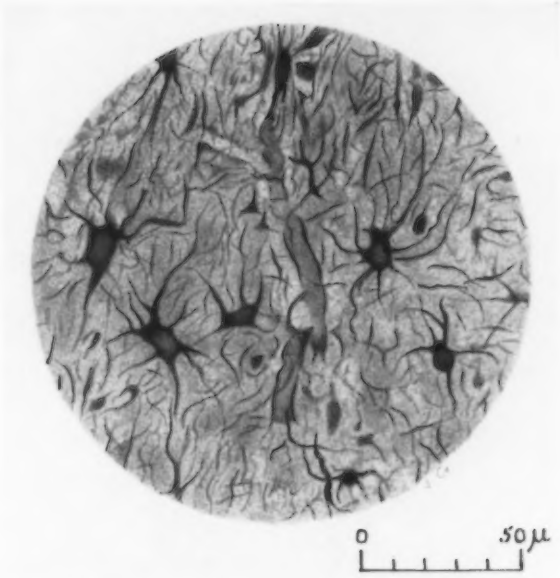

FIG. 3.—From the neighbourhood of the corpus callosum. The neoplastic astrocytes are large and numerous, and have reached a high degree of differentiation. Frozen section treated by Cajal's gold chloride sublimate method.

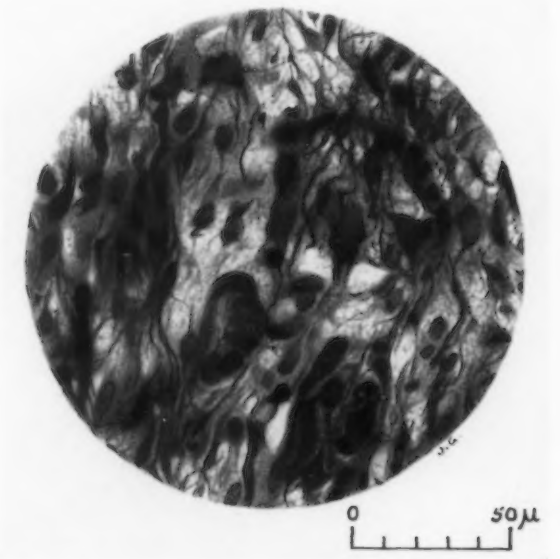

FIG. 4.—From the peripheral portion of the glioma. Some of the neoplastic cells are elongated, resembling the spongioblasts of the developing central nervous system. Frozen section treated by Hortega's silver carbonate method.

To illustrate paper by F. E. Reynolds.

involving a considerable portion of the white matter, but its limits were not well defined to the naked eye, the obviously neoplastic tissue merging into that which appeared "normal." A hæmorrhage rather more than 1 cm. in diameter was situated in the subcortical white matter in the neighbourhood of the precentral gyrus, 1·5 cm. below the surface; the extravasated blood was dark red in colour and the clot was very loosely held together. The tissue lying deep to the hæmorrhage was considered to be neoplastic, but that superficial showed no macroscopic change from the normal. (Later microscopic examination revealed, however, that neoplastic tissue was present superficial to the hæmorrhage, and had invaded the cerebral cortex.)

On the *left* side, the neoplasm had invaded the white matter of the hemisphere in a similar manner, but as far as could be seen it was not so extensive as on the right side.

Microscopical examination.—Portions of tissue were taken from each side about 2 cm. from the middle line, and, having been divided into pieces of suitable size, were fixed in Helly's modification of Zenker's solution. Thereafter the pieces were carried through the routine procedure for paraffin sections and were stained by Meyer's acid hæmatin and eosin and by Heidenhain's Azan method.

Pieces of tissue were taken from various portions of the neoplasm, including those near the corpus callosum and those near the periphery in the neighbourhood of the subcortical hæmorrhage and were fixed in formol-ammonium-bromide solution. Frozen sections made from these were treated by Cajal's gold chloride sublimate, by Hortega's silver carbonate and other silver impregnation methods, and by Morgan's method for demonstrating myelin sheaths.

(1) Sections of the more central parts cut in paraffin and stained by hæmatin and eosin and by the Azan method showed the neoplasm to be a glioma rich in nuclei. The nuclei varied in size, the average being considerably larger than that of a normal astrocyte, and they contained a large amount of chromatin.

Throughout the sections were many areas of necrosis. These areas consisted of a central mass of granular and structureless material surrounded by a zone in which the neoplastic nuclei were pyknotic and in various stages of disintegration. This appearance, therefore, was that frequently referred to by authors as the "palisade arrangement."

In many instances, the neoplastic cells immediately around a blood-vessel were not necrosed, but the tissue situated more distal had disintegrated; thus the picture presented in these portions was that of the so-called "pseudo-rosette" (fig. 2).

The walls of most of the arterioles were thickened, the thickening being chiefly in the inner coat, although considerable fibrosis was present in the muscular coat. In many cases, thrombosis of smaller blood-vessels had occurred and in some of these the thrombus had been organized into hyaline fibrous tissue.

(2) (*a*) Sections taken from the neighbourhood of the corpus callosum and

treated by Cajal's gold chloride method demonstrated this portion of the glioma to be composed of numerous large astrocytes which had reached a high degree of differentiation. Many of their processes were long and thick, and some of them were seen to come into relationship with blood-vessels, but vascular foot-plates were not well formed. Occasionally a fibre had developed in one of the processes, but for the most part the neoplastic astrocytes were of the protoplastic type (fig. 3).

At some distance from the main mass of the portion of the glioma involving the corpus callosum, small groups of fibrous astrocytes were seen which were large and with thickened processes, but which showed structural perfection; some of them contained two nuclei, being in a state of amitotic division.

At the periphery of the necrotic areas the neoplastic astrocytes were swollen and their processes were fragmenting ("clasmatodendrosis").

(*b*) Sections taken from the peripheral portions of the glioma, treated by Cajal's gold chloride and by Hortega's silver carbonate methods, demonstrated that differentiation of the neoplastic cells was not nearly so advanced as in the central portions. The nuclei were numerous and showed great variation in size, some of them being exceedingly large.

In certain areas some of the neoplastic cells were elongated, resembling the spongioblasts of the developing central nervous system (fig. 4). In other areas the structure was that of a syncytium, numerous large nuclei being embedded in a protoplasmic matrix (fig. 5).

The pre-existing astrocytes involved by these actively growing portions of the neoplasm were undergoing clasmatodendrosis (fig. 6).

(3) Sections of the peripheral portion of the neoplasm, stained by Morgan's method, showed that the myelin sheaths had disappeared in the neoplastic area. At the extreme periphery of the neoplasm a certain number of them persisted, but they were irregular in outline and the myelin had disintegrated into droplets.

(4) Sections of the peripheral portions of the neoplasm, stained by Gross-Bielschowsky's method, showed nerve-fibres persisting in the neoplasm for a considerable distance below the cortical layers, and a certain number of them were present in those portions of the neoplasm which were necrotic. In these areas many of the nerve-fibres present showed nodular swellings and were disintegrating into granules.

Commentary.

Many of the pathological problems raised by the case now published have been discussed in the paper by Slater and Reynolds to which references has been made already. To avoid needless repetition, these points will be referred to only so far as they require amplification in view of the differences in the histological picture of portions of the glioma which forms the subject of the present publication.

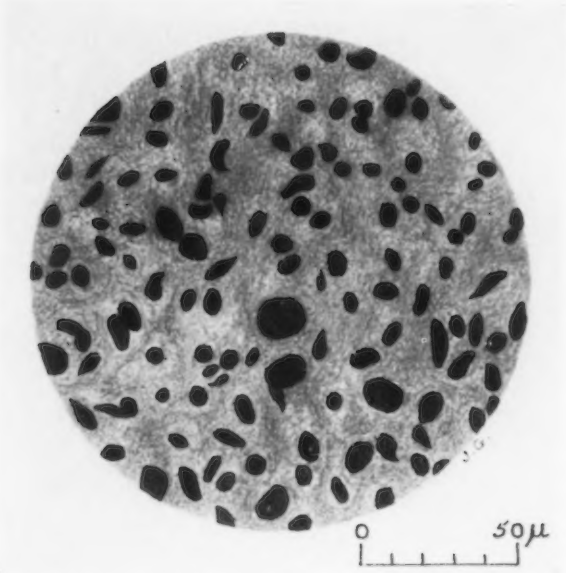

FIG. 5.—From the peripheral portion of the glioma. The structure is that of a syncytium, numerous large nuclei being embedded in a protoplasmic matrix. Frozen section treated by Hortega's silver carbonate method.

FIG. 6.—From the peripheral portion of the glioma. The processes of pre-existing astrocytes, involved by the actively growing neoplasm, are swollen and disintegrating ("clasmatodendrosis"). Frozen section treated by Cajal's gold chloride sublimate method.

To illustrate paper by F. E. Reynolds.

From the comparatively large amount of necrosis present, and the high degree of specialization reached by the neoplastic astrocytes, there is no doubt that the portion of the glioma in and around the corpus callosum was of older standing than the peripheral portions. Further, whereas the cells in the older parts had passed into a quiescent phase, the elements in the peripheral portions were in a very active vegetative condition.

The glioma had arisen, therefore, in the central portions of the brain and had extended widely in both cerebral hemispheres. The structure of the actively growing peripheral portions was largely that of a syncytium, and the only differentiation of the elements near the periphery was into cells, having as their prototype the spongioblasts of the developing central nervous system.

Hence the gliomatous elements showed all degrees of structural differentiation from the syncytium to cells having a very close resemblance to the fully developed normal astrocyte.

The demonstration of the manner of growth of the glioma which is the subject of the present paper, namely, a syncytial infiltration of the surrounding cerebral tissue, explains the difficulty experienced in differentiating by the naked eye between the normal cerebral tissue and the adjacent neoplastic glia.

It is probable that many gliomata grow as a syncytium. Veszpremi (*Virch. Arch.*, 213) maintained that in the majority of cases the glioma has a syncytial character in its actively growing peripheral parts, whereas in the older central portions the elements had differentiated into individual isolated cells.

Under the microscopic examination of the present case, it was noted that at some distance from the neoplastic tissue small groups of enlarged fibrous astrocytes were present, and that some of them were even in a stage of division. That these astrocytes were pre-existing cells and not those of an invading process of the glioma, which had been cut transversely, was concluded not so much from their position in relation to the neoplasm as from the structural perfection which they represented.

The significance and explanation of groups of astrocytes similar to those described has been discussed in the paper by Slater and Reynolds (loc. cit., p. 432).

The present case well illustrates the necrosis which is so common a feature in gliomata. Death of the cells is due probably to a number of factors; of these, an insufficient nourishment of the cells is present

in most instances and results, firstly, from the rapid proliferation of the neoplastic cells causing the tumour to outgrow the blood supply, and secondly, as demonstrated in this case, to thrombosis of blood-vessels in the neoplasm. On general principles, the thrombosis occurs owing to injury of the endothelium lining the lumen of the blood-vessel, and hence the question arises as to the nature of the agent which causes the damage.

It is an anatomical fact that every astrocyte, normal or neoplastic, has at least one, but probably more, of its processes which comes into relationship with the perivascular adventitial lymph sheath of the blood-vessel and which enters into the formation of the membrana limitans perivascularis. We are of opinion that as a result of this anatomical relationship, in the case of the astrocyte, absorption and excretion of metabolic substances occur through these processes (Reynolds and Slater, *Edin. Med. Journ.*, 1928, p. 54). During rapid reproduction of the cells, not only are metabolic products excreted into the perivascular lymph clefts in much larger amounts than under normal conditions, but in the case of neoplastic cells it is known that the chemical nature of their effete products differs from those of the normal cell. It is justifiable to presume that the mechanism by which the waste products are drained away, while sufficient for more ordinary conditions, cannot cope with the great excess of excretion. Consequently the fluid in the perivascular lymph spaces becomes saturated with these waste products, and we suggest that it is their presence together, possibly, with their altered chemical nature which is responsible for the damage to the vascular endothelium.

Lastly, it seems appropriate to discuss very briefly the classification of gliomata. Of late years, the tendency has been to divide these neoplasms into more or less numerous classes. These classifications are based on the varied histological picture presented by the neoplasms. But such a division is necessarily artificial and, as in the present instance, gliomata occur which present all stages of structural development, from the simplest—namely the syncytium—to the most complex—namely the astrocyte.

It seems better to us, therefore, to interpret the structure of gliomata along lines of progressive specialization of their elements as indicated in the present paper, rather than to attempt to allocate them to a particular structural category.

From the point of view of determining and interpreting the structure of a glioma, the present case illustrates the necessity, firstly,

of placing material of suitable size into fixative as soon as possible after death, so that it may be examined adequately by gold and silver impregnation methods; and, secondly, of examining different portions of the glioma.

Summary.

(1) The present study is of a large glioma cerebri which began in the central portion of the brain and extended widely into both cerebral hemispheres.

(2) The older parts of the neoplasm consisted of astrocytes which had attained a high degree of specialization, whereas the actively extending and recently formed portions were composed of a syncytium and of cells having as their prototype the spongioblasts of the developing neural tube.

(3) At some distance from the neoplastic tissue, there were small groups of pre-existing astrocytes which were proliferating.

(4) Necrosis in the neoplasm was due probably in part to its outgrowing the blood supply and to the accumulation in the tissues of the waste products of neoplastic metabolism.

(5) It is better to interpret the structure of gliomata along lines of progressive specialization of their elements rather than to allocate them to a particular structural category.

In conclusion, we desire to express our thanks to Professor Ritchie for giving us the opportunity of investigating the pathology of the case and for his permission to publish the results. We are indebted to the Medical Research Council for a grant towards the cost of the research and to the Carnegie Trust for financial assistance in publishing the illustrations.

THE CORPUS CALLOSUM AND ITS TUMOURS.

BY REDVERS IRONSIDE,
London,
AND
MANFRED GUTTMACHER,
Baltimore.

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Historical Introduction.

In the year 1675, Wepfer, the Professor of Medicine at Tübingen, published his famous "Apoplexia." In this book (Case history 14) is recorded what must be one of the first tumours of the corpus callosum ever reported. A perusal of this history gives a picture of the neurology of the era of Willis, Boerhaave, Haller, Sydenham, Morgagni, Valsalva and Meade, which is hardly equalled by the dissertations of any modern writer.

Ursula Aberlin, of Wolfach, a virgin, aged 23, was a maidservant to the innkeeper "At the Sign of the Sun." In the year 1667, one day she carried home from the field a ponderous bag of grain on her head. She suddenly had a sensation as though something had burst within her head. She was, however, able to continue uphill and perform her errand, but "from this time she was less capable of retaining her urine, yet no one excelled her in her accustomed duties as a servant-maid, neither putting off strenuous affairs to some other time, nor putting her labours upon her sturdier employer. Six months later," continues Wepfer, "having no presentiment of anything evil, at the hour when the cock crows, she thought herself unable to stand firmly

on her left foot. Her whole left side soon became deprived of motion and sensation, her lips were twisted, her maxilla deviated to the right. As soon as she was able, she spoke intelligently; indeed, only a short time after her very desperate state. She then lapsed into a delirium for several days and complained of the most raging pain in the top of her head, and the right eye pained most intensely, as though it were being evulsed from its orbit." Her frequency of micturition became more marked and there was, apparently, polyuria, without, however, incontinence. "On February 1, 1668, at the request of the illustrious Anna Magdalene, the Countess of Fürstenburg, I was called to see the girl. Eight weeks after her hemiplegic ictus she was still fat and of good colour, her mouth was no longer distorted and she spoke sensibly and quickly. She was no longer harassed by the intense headache. Although unable to move her left arm spontaneously, when one or other of her digits was forcibly flexed and compressed by me against the palm, she withdrew her arm a very little distance towards her.[1] She was unable to move her left foot. At that time, however, her left arm and leg were often flung up in a convulsive movement." Power gradually returned to her hemiplegic limbs, but six months later headache and giddiness returned. Gradual failure, with amenorrhœa, followed, and eighteen months after the onset of her illness "she grew delirious for many days," but just before her death she became rational. Always, even to her last breath, she saw and heard accurately. On March 24, 1669, she died. "By entreaty and money," says Wepfer, "I obtained the opening of the cadaver on March 25th." He found a cystic degenerating tumour of the posterior part of the corpus callosum, extending into the right lateral ventricle and the right internal capsule.

We have been able to find only one case report of an earlier date than this, reported by Felix Plater, Professor of Medicine at Basle, in his "Observationum," under the heading, "Stupor or Obfuscation from a Globular Tumour Occurring in the Brain." This case report is of some interest, as it gives an account of the apathy and lethargy characteristic of many growths of the corpus callosum. A study of the pathological report on this case, in the light of retrospect, indicates that the tumour was probably a hæmangioma of the falx, involving the corpus callosum.

"Caspar Bonecurtius, a Knight, gradually, over the course of two years, became mentally deranged, until finally he was utterly incapable of any reasoning. He did not ask for food and it was difficult to force him to eat; nor, unless coerced, did he seek his bed, but continually sat with his arms on the table, supporting his head with his hands. There he was wont to sit, almost asleep, neither asking questions nor volunteering any information spontaneously. Occasionally, he uttered a few words but they were hardly

[1] An interesting foreshadowing of Leri's reflex.

relevant. These things having gone on in this state for half a year, he suddenly died." At autopsy, a globular tumour "the size of a small apple" was found over the corpus callosum. It was composed of masses of tortuous venules.

Soye, in 1698, in the "Extraits du Journal des Savants," described a case characterized by epileptiform convulsions.

Morgagni, in 1740, in the "Epistolae" appended to the works of his great master, Valsalva, described a case with great mental slowness, lethargy, and gradually oncoming right-sided weakness; and in 1741, La Peyronie described two cases with lethargy, apathy and mental defect and, in one of the cases, epileptiform convulsions.

We see that, while some of the salient features of tumours of the corpus callosum have been known for nearly 300 years, these observations had no real pertinence in the historical development of the clinical diagnosis. Before Bristowe's establishment of the "Callosal Syndrome" in 1884, no serious efforts seem to have been made to make the diagnosis during life.

The first attempt to formulate a syndrome was that of J. S. Bristowe, who published his observations in this Journal forty-five years ago.

Bristowe stressed:—

(1) The ingravescent character of the symptoms—a progressive hemiparesis with vague motor symptoms on the contralateral side.

(2) The supervention of apathy, associated for the most part with extreme drowsiness, a puzzled, inquiring look, difficulty in swallowing and cessation of speech. He stated that this seemed due, mainly, to a stupidity and an irresistible tendency to sleep. He never noticed a true aphasia.

(3) The absence of cranial nerve palsies.

(4) The slightness of headache and vomiting.

This work remains the inspiration of all subsequent work on this subject, both in this country and abroad. In England and America less attention has been paid to tumours of the corpus callosum than on the Continent. Of recent years the most important contributions to the subject have been those of the Italian school, including Mingazzini's monograph, "Der Balken," published in 1922; a more recent paper by his pupil Balduzzi, in the *Archiv für Psychiatrie und Nervenkrankheiten*, in 1926; and Ayala's article, published in 1915.

The more important contributions of the French school are the Paris Thesis of Levy-Valensi, published in 1910, and the papers of

Raymond. To the "syndrome" of Bristowe, Schüpfer, in 1899, added the idea of localization within the corpus callosum, according to whether the neoplasm occupied the genu, the tapetum or the splenium. Raymond, in 1906, added a detailed account of the psychical changes which had been observed in tumours of the corpus callosum, and Liepmann, in 1907, described the symptom of apraxia in callosal lesions.

Balduzzi, in the most recent paper published in German, in 1926, reviews 115 cases of tumour of the corpus callosum, collected from the literature. Up to the present time no writer has contributed more than four individual cases. With the wealth of clinical material which is available at the National Hospital, Queen Square, London, and the Johns Hopkins Hospital, Baltimore, we are able to put on record in this paper fourteen additional cases previously unpublished. The diagnosis of tumours of this part of the brain has been made but rarely during life. The present paper is an attempt to define more clearly the symptomatology and signs of tumours in this region.

Anatomical Considerations.

The corpus callosum is the chief inter-hemispherical association system between the two halves of the neopallium. There are, however, other commissures, namely, the anterior commissure, the massa intermedia and the posterior white commissure, which may, as Lewandowski first pointed out, functionally replace a damaged, or partially destroyed, corpus callosum.

The corpus callosum is seen, on medial sagittal section of the brain, to form an arched structure about 10 cm. long. Its anterior end is about 4 cm. from the frontal pole, and its posterior end about 6 cm. from the occipital pole of the hemisphere. It is wider and broader posteriorly.

The superior surface is traversed by numerous transverse ridges and furrows, and is covered by a thin layer of grey matter, the indusium, which exhibits on either side of the middle line the medial (nerves of Lancisi) and lateral longitudinal striæ.

The medial striæ may be traced round the genu and rostrum to the gyrus sub-callosus. The lateral striæ may be followed into the area parolfactoria and the anterior perforated spot. Caudally, these striæ, as well as the indusium, pass round the splenium into the gyrus dentatus. The investing grey matter of the corpus callosum and the two sets of striæ represent the remnants of an atrophic olfactory convolution, which

has gradually been reduced in size as a result of the progressive development of the corpus callosum in mammals.

A corpus callosum may be observed in the animal series from marsupials to man, and its development in size is parallel with the phylogenetic development of the neopallium. With the assumption of the erect posture by the higher apes, olfactory sensations took a less prominent place than heretofore, and the rhinencephalon gave way to the development of inter-hemispherical association fibres connecting both halves of the neopallium, which was ever-increasing in size and complexity. Marshall pointed out that the corpus callosum was twice as large in man as in the chimpanzee, and he associated this with the development of the functions of speech, the development of psychical functions and the increase in size of the neopallium.

Spitzka found that the area, depth and length of the corpus callosum in higher apes, negroes and white people, increased with the degree of mental development. He found that the area of cross-section of the corpus callosum was greater in those of average intelligence than in the feeble-minded, and actually claims that measurements of the corpus callosum may indicate the degree of intelligence.

In man the corpus callosum, the fornix and the anterior commissure begin to develop about the fourth month of fœtal life. The lower part of a thickening in the lamina terminalis differentiates first into the anterior commissure, later into the anterior part of the fornix, and afterwards its posterior pillars are formed. Finally, the corpus callosum appears, its anterior part being the first developed, and its growth extending backwards with the development of the hemispheres.

Mingazzini's researches on the myelination of the corpus callosum in the human fœtus are of interest. He distinguishes three stages: (1) During intra-uterine life no myelin fibres can be seen in the corpus callosum. From the second week to the end of the second month of extra-uterine life myelination begins. (2) From the third to the seventh month myelination of the transverse fibres appears in the lateral regions and in the superior and inferior aspects of the corpus callosum. 3) Myelination becomes complete about the twentieth month of extra-uterine life. The longitudional fibres lying most medially are the last to become myelinated.

Mingazzini's studies show that the transverse fibres originate from large and small pyramidal cortical cells as association fibres: von Muratow says exclusively from large pyramidal cells. Other fibres represent the collaterals of long projection tracts, or are bifurcations of

association fibres. It may be taken as the current consensus of opinion that in the adult the commissural fibres connect homologous and heterologous cortical areas. This work of Mingazzini has recently been confirmed in the main by Villaverde. The *genu* contains fibres uniting the frontal convolutions of the two hemispheres. The *body* of the corpus callosum contains fibres uniting on the two sides, the first frontal and the pre-central convolutions, the parietal lobes, the paracentral lobules and the insulæ. The *splenium* contains fibres uniting the parietal lobes, the occipital convolutions, the lingual lobes and the angular gyri. In the main the transverse fibres constitute interhemispherical connections between identical areas of the brain.

One is reminded of the controversy which disturbed the neuroanatomists at the end of the last century. Meynert believed that the fibres connected only homologous areas of the hemispheres. He claimed that he had traced individual fibres from one side to the other, and his opinion was supported by Reil and Arnold.

One of the most important workers on the morphology of the corpus callosum was David Hamilton, the Professor of Pathology at Aberdeen. In 1885 he published the results of years of labour on the structure of the corpus callosum, enunciating the then heterodoxic view that the corpus callosum carried fibres to the opposite thalamus, caudate nucleus, internal and external capsules, the optic and olfactory tract and the temporal lobe. He believed that these fibres decussated in the midline, crossed to the external part of the corpus callosum, going upwards and outwards, and then turning downwards towards the lenticular nucleus, where they divided into an inferior group going to the internal capsule and a superior to the external capsule. Moreover, he failed to find positive evidence that the corpus callosum connected any two homologous cortical areas. Hamilton, modestly enough, gave Gratiolet and Foville priority for some of these views, but with them, however, they were really mere speculations, and, in all fairness, Hamilton must be called the originator of this doctrine. Hamilton worked on human adult and embryo brains. In this investigation he made use of his now forgotten method of "mezzoscopy." The brain was treated by gelatine and potash; the fibres swelled from one third to twice their normal size, so that they could be nicely distinguished by a hand lens.

In England, Beevor, supported by investigations on monkeys and marmoset embryos, opposed Hamilton bitterly. In 1899 Sherrington performed cortical ablations in monkeys, and found that, in the corpus callosum, fibres "tend to scatter and do not pass chiefly between

identical areas of the two hemispheres." These results were substantiated in 1901, by Lyndon Mellus working in Horsley's laboratory.

Bianchi and D'Abundo, as the result of cortical ablation experiments performed in 1886, on dogs and cats, postulated the existence of a tract going from the cortical motor area through the opposite internal capsule, returning to its original side by a lower crossing in the pyramidal decussation.

Wallenberg, working on the pole-cat, Bechterew and Ugolotti and von Mayendorf, all traced projection fibres to the opposite internal capsule, but Dejerine, and more recently Levy-Valensi in his "Anatomical Researches," published in 1910, were unable to demonstrate such projection fibres.

At the Düsseldorf Annual Meeting of the "Gesellschaft Deutschen Nervenärzte," held in September, 1926, Mingazzini, who for many years has kept a constant interest in this subject, read a paper—"The Relations between the Corpus Callosum, the Lenticular Fibres and the Internal Capsule." This was the result of a study that he had made with Gianelli on the brain of an idiot who had suffered since birth from a right spastic hemiplegia. They concluded that "a very considerable proportion of the corpus callosal fibres which originate from the right hemisphere bend round the left caudate nucleus and contribute to the formation of the left internal capsule."

The relation of the longitudinal tracts running under and alongside of the corpus callosum to its integral fibres is still unclear. It is most likely that (1) the fasciculus sub-callosus, and (2) the fasciculus occipito-frontalis, are structures entirely separate from it. The question as to whether the fasciculus callosum longitudinalis is a definite part of the callosal system is more uncertain.

In conclusion, one may state the present-day opinion as being (1) that the commissural fibres arise from large pyramidal, small pyramidal, and polymorphous cells of the cortex (Cajal) and unite homologous and heterologous areas of the two hemispheres; (2) that definite bundles of callosal projection fibres pass from the hemispheres to the internal capsule of the opposite side.

Physiological Considerations.

The corpus callosum appears to have been first recognized by Galen at the beginning of the first century A.D. Fifteen hundred years later this structure was selected by La Peyronie, the Professor of Surgery at Montpellier, as the "seat of the soul." La Peyronie's pronouncements

were received with great attention, and the stamp of finality seemed to be placed upon his hypothesis when Giovanni Maria Lancisi, physician of several Popes, gave it his support in his "De Sede Cogitantis Animae," which he wrote in 1718. By this time Willis had undertaken researches on the structure of the corpus callosum, and Sir Christopher Wren's beautiful engraving of Willis's dissection of the corpus callosum may be seen in the 1664 edition of the great anatomist's "De Cerebri Anatome."

In 1749, the experimental method of study of the corpus callosum was commenced by Haller's favourite pupil, Johann Gottfried Zinn, who published at Gottingen in his 21st year a brilliant monograph which is an orderly and logical piece of experimental work on the corpus callosum of dogs. He found that section of the corpus callosum produced lethargy and later paralysis of the limbs, at first confined to one side, later bilateral. As a result of the six experiments, however, he concluded that "the corpus callosum may be damaged and cut, yet the senses and power of movement remain intact." It is interesting to note, in reviewing his protocols, that lethargy seems to have been an almost constant symptom in his animals. Other earlier experimenters were Vieussens, Perrault and Karpius, Petit, Valsalva and Saucerotte. The results of these earlier workers were almost certainly marred by the occurrence of secondary infection.

Between 1830 and 1850, Lorry, Longet, Magendie and Flourens, all made total sections of the corpus callosum with negative results. The operation is by no means a simple one, and most workers have had a high operative animal mortality. The usual difficulties in appreciating psychical changes in animals are present. No recent worker has obtained clear-cut disturbances of motility following section, and the majority of workers—Franck and Pitres, and Dotto and Pusateri working on cats, Monaco and Koranzi on dogs, and Levy-Valensi on monkeys, have been unable to observe any effect on the psychic behaviour of their animals.

In 1893, Muratow published the results of his experiments on dogs, which fit in beautifully with our clinical experience of the effects of lesions in man. Only three of his animals survived section of the corpus callosum. He found these animals sleepy and apathetic. They were badly orientated and paid no attention to their surroundings. They maintained uncomfortable postures in which they were placed. Their gait was inco-ordinated and uncertain. They did not appear to see obstacles placed directly in front of them and stumbled over them. Although Levy-Valensi has produced an essentially similar picture in

dogs—stupidity and apathy, the forgetting of many tricks and apraxia—by longitudinal section of the corpus callosum, we may hesitate to accept these results without further confirmation.

In 1887, Brown-Séquard performed electrical stimulation of the corpus callosum; he found that the current had to be stronger than that needed to excite the Rolandic area, and he concluded that every part of the corpus callosum had fibres capable of giving movements on stimulation.

Lewandowski put forth the theory that the corpus callosum is the pathway by which the stimulus giving rise to an unilateral convulsion spreads to the opposite hemisphere, but Franck and Unverricht found that section of the corpus callosum in animals plays no part in preventing a convulsion from becoming generalized.

Between 1900 and 1908, Liepmann published a series of brilliant papers in which he pointed out the predominant influence exerted in man by the left hemisphere, and the value of apraxia as a diagnostic sign of callosal damage. Certain functions of the limbs acquired by experience and practice and comparable to the functions of speech, have their cortical centres situated in the left hemisphere, these centres being connected with the corresponding centres in the right hemisphere by means of the anterior fibres of the corpus callosum. Apraxia may be purely motor, or it may be sensory in origin, due to failure of recognition of objects, just as agraphia is produced by visual agnosia of words.

Over 95 per cent. of people are right-handed. In them the left cerebral hemisphere is the dominant one, and besides controlling the limbs of the right side of the body, exercises a potent influence upon the right cerebral hemisphere by means of the commissural fibres of the corpus callosum. Thus, many movements of the left limbs are initiated through the corpus callosum by the left hemisphere, so that a left-sided brain lesion, if implicating callosal fibres, may produce not only a right-sided hemiplegia but also apraxia of the non-paralysed left side. This was the first serious contribution to the physiology of the motor functions of the corpus callosum.

According to Wilson [*Brain*, 1908] three clinical varieties of apraxia may be met with: (1) A *sensory* form of apraxia where the patient, when shown an object, is unable to use it in the correct fashion, because the idea in the patient's mind of the nature of the object is incorrect, i.e., there is visual agnosia. Thus, a person shown a pair of scissors and asked to use them may not recognize the scissors as such, and may

perhaps convey them to his mouth as he would a fork. (2) An *ideational* type of apraxia where the patient recognizes objects, but through want of attention or defective retentiveness of memory is unable to execute the main idea of the movement. A man, shown a matchbox and a candle and asked to use them, may put the candle in his pocket and open the matchbox, recognizing and naming the objects, but unable to grasp and execute the main idea suggested to him, viz., to light the candle. (3) A *motor* type of apraxia, where objects shown are recognized and commands given are understood, yet the latter cannot be executed. Although the general idea of the action is understood and there is no paresis, the normally worked out idea cannot be exteriorized. Thus, an apraxic patient with a right hemiparesis, asked to make a military salute with his left hand, although comprehending what is needed of him and having no paralysis of his left upper limb, is unable to exteriorize the idea of the movement.

The excellent studies of Charles Foix and Pierre Hillemand on "Lesions of the Anterior Cerebral Artery" have done much to enlarge our knowledge of the functions of the corpus callosum and have given us a clear picture of callosal apraxia. The anterior cerebral artery supplies the anterior 7/8 of the corpus callosum by branches arising from the concavity of the callosal arterial arch. This artery supplies also the orbital lobule and the prefrontal lobe and all the medial aspect of the cortex except the occipital supply of the posterior cerebral artery. On the lateral aspect of the hemisphere it supplies the first frontal convolution, the superior part of the two Rolandic convolutions, and the parietal convolution near the inter-hemispherical fissure. Besides this, the artery supplies the centrum ovale in the neighbourhood of the caudate nucleus and the head of the caudate nucleus itself.

Cortical or subcortical lesions of this artery, associated with arterial obliteration of the anterior cerebral supply of the centrum ovale, produce monoplegia or hemiplegia with weakness predominating in the lower extremity. When, however, destruction of the callosal arterial supply occurs with softening of the anterior 7/8 of the corpus callosum, *left-sided motor apraxia* is added to the above syndrome. The apraxia is not met with unless there is softening of the corpus callosum, and the apraxic syndrome is always on the left side, irrespective of the side of the arterial lesion. These authors point out that this *left-sided, unilateral motor apraxia*, met with in callosal lesions, differs from the apraxia met with in lesions of other parts of the hemispheres. In lesions of the parietal and supra-marginal gyri the apraxia is bilateral

and of the ideo-motor type, and is associated with right hemiplegia, aphasia, and perhaps also hemianopia and sensory loss. In lesions of the temporal lobe apraxia may also occur, but it is of the ideational type and associated with further psychical disturbances. These workers have thus established the distinction of callosal apraxia from other forms, and have shown the predominance of the left hemisphere in the normal eupraxia of movement.

La Fora and Prados performed an interesting series of experiments in 1921 on this subject. They trained a series of male cats and monkeys of both sexes to perform rather complicated movements requiring certain special movements of the left fore-limb, while they reached for food with the right. After each animal was thoroughly trained its corpus callosum was cut. These workers had uncommonly bad fortune with their surgical results, and those animals which did survive seem apparently to have gone through such a stormy period of convalescence that the procedures taught had been forgotten. This approach, however, would seem a logical one, particularly if one employed the higher apes which are, according to Henschen and Kohlev, predominantly right-handed.

Hartmann and Trendelenburg published a series of experiments of a somewhat comparable nature in 1927. Of the ten apes upon which they operated only four survived. In only one of these were they successful in performing a complete section of the corpus callosum. They found no evidence of apraxia in their animals.

The study of conditioned reflexes in animals by Pavlov and his co-workers has done more to clear our ideas regarding the functions of the corpus callosum. Bykoff has shown that in dogs a differentiation of the direction of a sound requires a united activity of both hemispheres. In normal dogs the differentiation of sounds by their direction presents no more difficulty than any other differentiation, and is capable of great precision. Salivary secretion reflexes conditioned by sound of a given pitch coming from a certain direction are easily established. If, however, the corpus callosum be sectioned and new conditioned alimentary reflexes established, the dog is unable to make any differentiation of the direction of the sound. "Other differentiations were obtained in this dog easily and rapidly, but never one involving localization of the source of the sound" (Anrep).

Tactile conditioned reflexes, which were developed from different places on one side of the body, reproduce themselves with surprising accuracy on symmetrical places of the other side of the body. Anrep

demonstrated this both for positive and negative reflexes to tactile stimuli. Bykoff found that after section of the corpus callosum conditioned reflexes to tactile stimulation of the two sides became entirely independent of one another. We may also refer to the work of Anrep on "The Irradiation of Conditioned Reflexes" (*Proc. Roy. Soc.*, B, 93, 1923).

These experiments are of great importance in showing that the bilateral synergic activity of the hemispheres may be dependent on the corpus callosum, and indicating the part which the corpus callosum plays in the development of symmetrical reproduction of function in the hemispheres.

In conclusion, one may summarize the hypothesis of Mingazzini, formulated in his monograph, "Der Balken." In the anterior third of the corpus callosum (portio verbalis et praxica) run fibres connecting the motor speech centres, and aiding in the harmonious functioning of these areas (und zur Ergänzung der Sprachfunktion beitragen). The middle and part of the anterior third of the corpus callosum (portio praxica) contain fibres connecting the cortical areas for stereognosis, the measurement of muscular movements and certain forms of deep sensibility, the visual and auditory areas in both hemispheres, which make possible co-ordination and harmonious working of the limb movements, e.g., as in painting a picture or in playing a musical instrument. The posterior third (portio sensorialis), including the splenium, is of greatest size in man, a fact which is associated with the development of larger cortical centres for vision and hearing and their commissural connections. This posterior third contains fibres connecting these cortical areas with the motor and speech centres, making possible eupraxia of speech, voluntary action, mimicry, &c.

He supposes that the corpus callosum has a psychical function consisting in the association of ideas formed in the cortex of both hemispheres, and thus permitting of a harmonious combination of these ideas; and he states that the psychical disturbances arising from lesions of the corpus callosum are to be ascribed to an interruption of the co-ordinating pathways. This supposition is shared by Gand, Hitzig, and also by Cajal. There are, of course, cases where despite a lesion of the corpus callosum no psychical disturbance resulted, and Mingazzini explains this on the hypothesis that the lower commissural systems take over its function and substitute for it.

Discrepancies between Physiology and the Known Clinical Picture of Pathological Lesions.

We see that whatever knowledge we possess of the physiology of the corpus callosum is partly hypothetical and the result of suppositions arising from anatomical findings. The results of clear-cut vascular lesions have contributed largely to our knowledge. Only in the recent experiments of Bykoff and Anrep has a purely physiological approach to the problem been made.

We may say unhesitatingly that the study of neoplasms of the corpus callosum will throw no light whatever on the physiology of that structure. Lesions produced by neoplasms differ in this respect from more clear-cut vascular lesions. There are grave discrepancies in the syndromes produced by tumours and those produced by experimental section of the callosal fibres. Every neuropathologist has observed the gross infiltration of nerve tracts by tumour tissue with the preservation of many microscopically intact fibres.

The lethargy and apathy of patients with callosal tumours have been produced in dogs, but these symptoms must be evaluated as they arise in animals which have been subjected to any mechanical cerebral interference. The quadriplegia, characteristic of the tumour syndrome in man, is not a marked feature after section of the corpus callosum in animals. Again, in vascular lesions producing softening of the corpus callosum there is no mention in recorded cases of any psychical change comparable to that which one associates with the tumour syndrome. In our study of neoplasms of this region of the brain we have been unable to confirm that apraxia is a frequent symptom. Some of our case records date back to a period before the publication of Liepmann's paper in 1907, and in some of the cases, admittedly, apraxia may have been present but obscured by the lethargic condition of the patient.

Taking into account the completeness of the case records, our series of tumour cases would lead us to believe that apraxia is not a common symptom of tumours of the corpus callosum.

The symptoms in corpus callosum tumours are largely of the "neighbourhood" type and arise from involvement of, or pressure on, adjacent structures by the growth.

Report of Fourteen Case Histories.

In the 1893 edition of his textbook, Gowers states "the chief lesion that occurs in the corpus callosum is tumour, but this almost always

extends into one or both hemispheres. Mental dullness and stupor, with weakness in the limbs, greater on one side, have been present in many cases, and in some there has been disturbance of speech and locomotion; but it is probable that these symptoms (with the possible exception of the mental dullness) are due to the pressure on, or extension into, the cerebral hemispheres. We do not yet know of any symptoms that are the result of the damage to the callosal fibres." In a footnote he refers to the four cases described by Bristowe in this Journal in 1884. Bristowe's paper was an attempt to emphasise the peculiar mental state, associated with progressive hemiparesis on the one side and "vague symptoms on the other," which characterizes these cases, and he attempted to stress other points, e.g., the absence of cranial nerve palsies and the paucity of general symptoms which might give a clue in making the diagnosis during life.

The fourteen cases which we are recording here have been carefully selected as being neoplasms apparently originating in, and largely confined to, the corpus callosum. Frontal tumours and occipital tumours extending into the corpus callosum, have been excluded. A study of these cases leads us to emphasize certain groups of symptoms which define with greater clearness the clinical picture of tumour of the corpus callosum.

(1) Hemiplegic weakness with pyramidal signs on the opposite side is frequent and early. Whereas great stress has been laid upon apraxia as a physical sign, it is not a prominent feature of our cases and is found probably in hardly more than 10 per cent.

(2) The mental changes which are so commonly present are often the first symptom. Apathy, drowsiness and defect of memory, are met with more commonly than in growths elsewhere, and occur with such regularity in the corpus callosum syndrome as to be characteristic.

(3) Epileptiform convulsions, in our series, are relatively frequent and attention may be drawn to the presence of other involuntary movements, tremor and choreiform movements, which are noted throughout our cases.

(4) The occurrence of yellow cerebrospinal fluid in four of the cases is, in our opinion, a point of considerable importance.

(5) In the main the general symptoms of cerebral tumour have been in abeyance, so that the diagnosis arrived at during life, in most of the cases here recorded, was that of cerebral vascular disease.

Gowers' statement that "the symptoms (with the possible exception of mental dullness) are due to pressure on to, or extension into, the

cerebral hemispheres," we believe still holds. In the light of physiological work summarized in a previous part of this paper, we have little doubt that the early psychical changes exhibited by these patients are largely due to interruption of the association fibres in the corpus callosum.

I.—Cases illustrating Early Hemiplegia with Later Appearance of Pyramidal Signs on the Opposite Side.

Case 1 (*National Hospital, Queen Square, London*).—*Tumour in posterior two-thirds of corpus callosum. Fairly sudden onset with left hemiplegia and drowsiness. First seen in Out-Patient Department with bilateral pyramidal signs. Later, mental changes and increasing drowsiness. Pupils unequal. No papilloedema or vomiting. No apraxia. Yellow cerebrospinal fluid.*

Morris E., aged 61. Admitted under Dr. Stewart, September 19, 1919.

Two months before admission patient's wife noticed he had weakness of the left side although he had had no fit or loss of consciousness. Seen in the Out-patient Department by Dr. Grainger Stewart a week later the abdominal

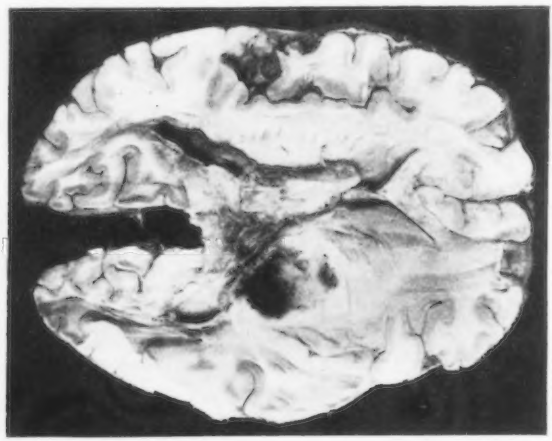

FIG. 1 (*Case* 1).—Tumour occupying the splenium of the corpus callosum and invading the right centrum ovale and fornix. The right lenticular nucleus is replaced by a solid mass of growth. The tumour surrounds the posterior horn of the right ventricle but does not invade it, and appears over a small part of the wall of the posterior horn of the left ventricle.

reflexes were absent, the tendon reflexes brisker on the left side than the right and both plantar responses extensor. The weakness of the left lower limb became progressively worse. His wife states that since his illness commenced he would fall off to sleep in the middle of a conversation.

One week before admission he became "light-headed," more drowsy and apathetic and he constantly patted the right side of his head, although there had been no complaint of headache and no vomiting had occurred.

On admission the patient could be induced to answer questions and there was no aphasia or apraxia. The optic discs and fundi were normal; there was left-sided visual inattention. There was slight left hemiparesis with marked weakness of the left face on emotional movement. There was left hemianæsthesia to cotton-wool and pin prick, and the left corneal reflex was diminished. The tongue was protruded to the left. The abdominal reflexes were absent, the tendon reflexes of the arms brisker on the left than the right. The knee-jerks were brisk and equal and the ankle-jerks greater on the left side. Both plantar responses were extensor.

Later the patient became more drowsy and the left-sided weakness became more marked. The plantar responses were variable. The left pupil became much larger than the right and there was constant conjugate movement of the eyes to the right. A week later there was spastic weakness of the right upper limb and some head retraction.

Cerebrospinal fluid.—Yellowish with coagulum, contained 2 cells (large lymphocytes) per c.mm.; albumin, 0·06 per cent.: chlorides, 0.69 per cent.; good reduction of Fehling; Wassermann reaction negative.

October 11, 1919.—Right parieto-temporal decompression. The patient died three days later.

At autopsy a tumour was found occupying the splenium of the corpus callosum, extending into the right centrale ovale (see fig. 1).

This case was characterized by the ingravescent onset of left hemiparesis, with later absent abdominal reflexes and the appearance of an extensor plantar response in the right as well as the left foot. Drowsiness and apathy were early symptoms in spite of the absence of headache, vomiting and papillœdema. But for the condition of the cerebrospinal fluid, it is possible that he might have been regarded as a cerebral vascular lesion. The bilateral pyramidal signs appeared to be due simply to the median position of the growth, and the predominance on left side to an extension of the growth into the right centrum ovale. The dilatation of the left pupil, the conjugate movements of the eyes to the right and the head retraction, are worthy of note.

Case 2 (National Hospital, Queen Square, London).—Tumour of the middle and posterior thirds of the corpus callosum. For three weeks bouts of irritability. Gradual onset of right-sided weakness and tremor. Progressive defect of memory with perseveration and aphasia. No apraxia, although involvement of the middle of the corpus callosum. Headache, vomiting and papillœdema. Right visual inattention. Pupils unequal. Later, bilateral pyramidal signs. Yellow cerebrospinal fluid. Decompression.

James H., aged 53. Admitted under Dr. Taylor, September, 19, 1919.

Three weeks before admission patient complained of severe occipital headache, worst in the morning, and had one bout of vomiting. He became very irritable and gave up work. Ten days before admission he began to lose the use of the right arm and leg. The weakness of the arm was slight, and his wife observed that the limb was tremulous when he held a cup of tea. About this time his speech became indistinct. Six days before admission his memory began to fail, he could not remember the date, and this had become progressively worse. He had difficulty in choosing the right word and would, for instance, ask for a halfpenny when he wanted his pipe.

Patient, on admission, was quite conscious and lay in bed occasionally talking to himself. He was completely disoriented in space and time. His spontaneous speech was almost unintelligible, and he used jargon words, e.g., called soap "choif," but answered questions normally and executed spoken commands correctly but with a tendency to perseverate in his actions. Asked to repeat words and phrases, he again perseverated in his answers. He did not appear to comprehend written commands, and read print aloud only with difficulty. He gave no response when asked to write spontaneously and could not copy the word "James," but he wrote to dictation the word "petrol" in printed capitals in a tremulous hand; i.e., he was definitely aphasic, chiefly on the motor side, with perseveration of speech and actions, and probably some alexia. There was no apraxia—tested with matchbox, key and various other articles. The optic discs were swollen to four dioptres, with striate hæmorrhages in both eyes, and there was right-sided visual inattention. There was a slight right hemiparesis and a fine tremor of the outstretched right hand. The tendon reflexes were all brisker on the right side. The abdominal reflexes were absent on the right side, and the right plantar response was extensor. The left upper abdominal reflex was not elicited.

A week later the general intelligence became much more impaired, the left pupil was larger than the right and did not react to light or on accommodation. Both plantar responses were now extensor and the abdominal reflexes absent on two sides. There was marked general tremulousness, and he became incontinent of urine and fæces. A week later he became intensely drowsy, and a lumbar puncture was performed.

Cerebrospinal fluid.—Yellow fluid 10 cells per c.mm. (large and small lymphocytes); albumin 0·06 per cent.; chlorides 0·74 per cent.; reduced Febling; Wassermann reaction negative.

A left temporo-frontal decompression was performed on October 3, 1919, by Mr. Armour. After this the plantar responses became flexor and the incontinence lessened, but the patient succumbed on October 14.

At the post-mortem a large tumour was found occupying the middle and the splenium of the corpus callosum and all the region of the left optic thalamus. The tumour invaded the posterior part of the lenticular nucleus and almost obliterated the left lateral ventricle, the middle portion and posterior horn of which it invaded.

In this case the presence of headache, vomiting and papillœdema made the diagnosis of cerebral tumour obvious. The yellow cerebrospinal fluid would suggest a proximity of the growth to the ventricles, and the bilateral pyramidal signs a median localization. The right visual inattention was probably due to an extension of the growth towards the left optic radiation, and the tremor due to extension towards the basal ganglia. This case, like the previous one, showed inequality of the pupils. The absence of apraxia, although the patient was right-handed and had a right hemiparesis, is noteworthy.

Case 3. (*National Hospital, Queen Square, London*).—*Tumour of the middle of the corpus callosum. Six months' history of gradually increasing lef hemiparesis, commencing in the leg, with loss of memory and apathy. Later left-sided Jacksonian attacks and quadriplegia.*

Rose M., aged 12. Admitted under Dr. Hughlings Jackson, April, 4, 1896; died April 18, 1896.

Until six months ago patient was bright and merry. Gradual languor began to overtake her, with some dragging of the left leg. Three months later the left upper limb became paralysed, and by this time she was said to have become stupid and had no memory.

She was admitted comatose after a left-sided fit the previous day. Fourteen days before admission she began to suffer from vertical headaches and vomiting

On examination the patient was fairly well nourished, comatose, with slight bilateral proptosis. She could just be roused by shouting. Both optic discs were swollen to the extent of one dioptre. The left pupil was larger than the right and both pupils dilated when a beam of light was directed towards them. There were slow lateral movements of the eyes—no facial asymmetry. Both upper and lower limbs were flaccid and extended, and it was noticed that the weakness was greater on the left side. The knee-jerks could not be elicited; the plantar responses were absent. There was incontinence of urine and fæces.

Fourteen days after admission patient died, and at autopsy a degenerating tumour was found occupying the middle of the corpus callosum.

In cases where all four limbs are involved, paralysis is usually of the flaccid type. Case 1 is an exception. It is interesting to note that in the case recorded above, as well as in the two previous cases, the pupils were unequal. In this case Jacksonian convulsions occurred.

Case 4 (*National Hospital, Queen Square, London*).—*Tumour of splenium. Fairly sudden onset with progressive agraphia and right-sided weakness. Progressive memory defect and drowsiness. No apraxia. Inconstant coarse tremor of the trunk and lower limbs.*

Henry L., aged 62. Admitted under Dr. Holmes, September 24, 1925.

Three weeks before admission patient's sister noticed that his letters to her were incoherent; words were left out and he omitted letters in spelling words. His handwriting was becoming illegible. She went to the Isle of Wight, where he was staying, and found that he had developed some weakness of the right arm and leg. She was struck by his slowness of thought and utterance, his loss of memory and his drowsiness. He could express himself with a little help, and he was still able to dress himself and perform the necessary daily offices of attending to his wants.

Although drowsy during the day, he was kept awake at times during the night by violent vertical headache which had come on two days previously. No vomiting. He was a healthy and vigorous man and until recently used to follow the hounds on foot.

On admission patient was semi-comatose. He could be roused with difficulty but did not comprehend questions or commands. His answers were monosyllabic and practically unintelligible. The right hand lay limply at the side and fell with a thud when raised and allowed to drop. There was slight right facial weakness. Occasionally a sort of shuddering tremor spread over the body. The respirations were periodic.

The patient was obviously aphasic; there had been no apraxia and no fits. Both fundi showed arteriosclerotic changes in the vessels, with blurring of the disc margins but no definite swelling. There was an inconstant coarse tremor of the trunk and proximal parts of the lower limbs. All the tendon reflexes were elicited more briskly on the right than on the left; the right plantar response was extensor, and all the abdominal reflexes absent. The patient was incontinent of urine and fæces. The blood-pressure was 158 98 mm. Hg; the second aortic sound was accentuated and hollow.

The blood-urea was found to be 57 mg. per 100 c.c. There was no albuminuria. The urea concentration test gave normal results. The Wassermann reaction in the blood was negative.

Patient died on October 16, 1925, twenty-two days after admission. At autopsy a tumour was found occupying the splenium of the corpus callosum.

The similarity of the clinical picture in this case to that of cerebral arteriosclerosis is striking. The rapid progress of the symptoms and the relatively slight arteriosclerosis visibly present, with the occurrence of bilateral pyramidal signs and bouts of coarse tremor in the upper and lower limbs, suggested a median neoplasm.

In the hemiparesis of corpus callosum tumours, Steinert has noted a predominance of weakness in the lower limb. This is confirmed by our experience. In most of the cases here recorded the weakness affected first one side, chiefly in the leg, and later spread to the lower limb of the opposite side. Paraplegia was not observed.

II.—*Cases illustrating Early Psychical Changes.*

Psychical changes of a particular kind are the most characteristic feature of our group of tumours of the corpus callosum. Their extreme frequency has been emphasized by other authors. In 110 cases collected by Mingazzini, they were absent only in 8; of 116 cases collected by Balduzzi, they were absent only in 10. They commence early and progress rapidly, and a condition is soon reached in which the mental changes dominate the clinical picture. The early stages are characterized by poverty of movement and thought, with lack of spontaneity. Torpor, apathy and depression, with loss of memory, characterize the early stages. Later, hallucinations may arise, the patient becomes disoriented, indifferent to his surroundings and to emotion. The last stages are characterized by dementia, interrupted by periods of transient motor excitement. The variability in the mental state from day to day is well recognized in the literature. We are in agreement with Stern, who believes that psychical changes are infinitely commoner in tumours of the corpus callosum than in tumours in other regions of the brain. The psychical changes may occur at a stage when there is very little increase of intracranial pressure. In the later stages, the mental symptoms due to involvement of the corpus callosum are difficult to separate from those due to increase of intracranial pressure.

Case 5 (National Hospital, Queen Square, London).—Tumour of the splenium. Gradual onset with general debility of twelve months' duration. Uncinate fits. Signs of increased intracranial pressure. Gross memory defect for recent events. Disorientation. Statuesque gait and tremor of the right upper limb; bilateral pyramidal signs. Yellow cerebrospinal fluid with increase in albumin and cell count.

Marian H., aged 46. Admitted under Dr. Collier, February 20, 1922. One year ago patient began to show signs of fatigue, apathy and depression. She complained frequently of bad tastes in her mouth, and for a few days before admission she complained of feeling "a horrible smell" in her nostrils at times. Five weeks before admission she complained of frontal headache and her husband noticed a failure of memory which lasted only a few days.

Seven days before admission her memory again failed; speaking to her husband she would say "Where is my husband? Oh! are you Fred?" The right upper limb began to shake and three days before admission she vomited. The patient was previously a healthy woman.

On examination, there was great failure of memory, especially for recent events, and she could give no account whatever of her illness. She was disoriented in space and time and could not tell how many days she had been in hospital, although she had arrived that afternoon. She could not remember

who had brought her and could not tell what day of the week it was. She could not tell her name, her age, or the number of the house in which she lived, although with difficulty she remembered the year of her birth and the name of the street she lived in. She stated that she had had no vomiting although she had had a severe attack three days before, which she had apparently forgotten.

She showed a tendency to repeat phrases or remarks during the examination and complained of feeling exhausted. The expression was vacant and abstracted.

FIG. 2 (*Case 5*).—Sarcoma occupying the posterior part of the corpus callosum and extending on either side of this, widely separating the posterior horns of the lateral ventricles. Exposed from above.

R. V. $\frac{6}{18}$; L. V. $\frac{6}{12}$. Fields of vision showed left visual inattention. Both the discs showed papilloedema, R.O.D. + 2, L.O.D. + 2, retinal veins tortuous. The right pupil was larger than the left. Both pupils reacted to light and on accommodation. The other cranial nerves were normal.

Both hand-grips were equally feeble. The right upper limb showed a tremor of fairly wide range, rhythmic and slow, seen when the arms were outstretched. With the finger-nose test the tremor was intensified towards the end of the movement. There was no sensory defect and no change in the tendon reflexes. The upper and lower abdominal reflexes were absent; the plantar responses flexor in type. The gait was statuesque and the patient leaned slightly backwards. There was slight general rigidity and the head was held tilted to the left. Patient did not swing the arms in walking, and the right upper limb was held slightly in front.

Ten days later both plantar responses were extensor. Dr. Collier saw this patient on March 5, 1922, and was of the opinion that the tremor was a spontaneous movement produced by pressure on, or lesion in, the left posterior lenticular nucleus, and that the loss of memory was due to a tumour of the splenium.

The cerebrospinal fluid was slightly yellow. There were 66 cells per c.mm. (mononuclears and polymorphs). The amount of total protein was 0·07 per cent. Nonne-Apelt positive. Lange, 0001110000.

Operation March 7, 1922 (Mr. Sargent). A left parieto-temporal craniotomy was performed. There was little increase in intracranial pressure. A probe was inserted into the middle temporal gyrus in a slightly upward direction and met with resistance at the depth of about an inch. An incision was then made in the posterior part of the middle temporal gyrus, but no growth could be discovered.

At autopsy, horizontal section of the brain at the level of the superior fibres of the corpus callosum showed a tumour occupying the posterior third of the corpus callosum and extending on either side of this, 4 cms. into the right hemisphere and 4·5 cms. into the left, in the direction of the biceps major. The growth was symmetrical and heart-shaped (apex forwards) extending towards the optic thalamus and pushing into, but not invading, the posterior horns of both lateral ventricles. The two halves of the choroid plexus were widely separated by the growth and lay in close apposition to the lateral walls of the body of the ventricles. The anterior horn of the ventricles showed no distension. The tumour extended for the most part posteriorly and laterally to the corpus striatum in the direction of the optic radiation. (See fig. 2.)

This case is a beautiful example of a tumour of the splenium diagnosed during life, illustrating the early onset of apathy and depression long before the onset of signs in the limbs. The failure of memory for recent events led to the patient's statement that she had had no vomiting, although she had had a severe attack three days previously.

Dr. James Collier has seen a case in which the patient was crying out with severe headache and holding his head, and when seen ten minutes later, when the headache had passed off, had apparently completely forgotten and emphatically denied having suffered from headache during his illness. Many authors have commented on the vacant and abstracted facial expression of these cases.

Besides the characteristic mental picture, this case also exhibited bilateral pyramidal signs, fits, tremors, inequality of the pupils and yellow cerebrospinal fluid, as in the majority of our cases.

The two following cases showed early depression and apathy.

Case 6 (National Hospital, Queen Square, London). — Tumour of the anterior and middle thirds of the corpus callosum, causing distortion of the anterior horn of right ventricle. Four months' history of general weakness, depression and apathy. Three months ago patient had a fit, which was followed by a progressive left hemiparesis. Dull on admission, with gross swelling of both optic discs. Left attentional hemianopia. Bilateral pyramidal signs. Static tremor of right upper limb. Yellow cerebrospinal fluid.

Edward M., aged 49. Admitted under Dr. Holmes, May 17, 1926. The patient was well until three months before admission, when he began to have "fainting attacks," which sometimes caused him to fall down. These attacks were followed by vacantness and disorientation lasting several hours, and it was noticed that between his attacks he had become depressed and mentally much duller.

The fainting attacks continued, and in these his left arm and leg would sometimes shake. He had one severe attack of vomiting and two generalized epileptiform convulsions. He complained of frequent severe headaches and blamed these for the recent loss of memory which had been noticed by his friends.

One month before admission he began to lose the use of his left arm and leg, and his speech was occasionally incoherent. This left-sided weakness had been becoming progressively worse.

On examination, the patient was extremely apathetic and mentally slow. It was impossible to elicit any history from the patient himself, as he could not remember the details of his illness. The speech was slow but there was no aphasia. The optic discs showed tortuosity of the arteries with increase of central light reflex. The outline of the discs was clear and they were of good colour. The pupils were equal and reacted normally. The external ocular movements were full but convergence was not sustained. There was marked left lower facial weakness, more on voluntary than emotional movement. The tongue, when protruded, deviated slightly to the left. There was almost complete left hemiparesis, the lower limb being completely paralysed, the upper limb preserving only feeble finger movements. The left lower limb was flaccid, the tone of the left arm slightly increased. There was no sensory loss. All the tendon reflexes were brisker on the left side. The left upper and lower abdominal reflexes were absent. The left plantar was extensor, with a marked withdrawal reflex.

The patient became much more drowsy, with incontinence at times. At one period, for twelve hours, he had intermittent twitching of the right face and upper limb. It was noticed that he lacked spontaneity. He would not speak or move unless commanded. There was fairly frequent static tremor, coarse and rapid in the right upper limb, and he developed left-sided attention hemianopia. It was noted that "the patient scarcely makes any spontaneous utterance, his face is blank, sunken and drawn."

The cerebrospinal fluid was yellowish, containing eight cells per c.mm. and

0·3 per cent of albumin. The Nonne-Apelt test was positive; Pandy test positive; Lange curve 0000011221. The Wassermann reaction was negative in the cerebrospinal fluid and blood. The cerebrospinal fluid contained 62 mg. per cent of urea.

Before death the patient developed slight swelling of both optic discs, in the right eye + 4 D. and in the left eye + 1½ D. The systolic blood-pressure measured from 145 to 132 mm. of mercury; the diastolic was 90 mm.

At autopsy a tumour was found attached to the falx cerebri infiltrating the corpus callosum about its centre and embedded in the right callosal convolution. The left callosal convolution was compressed but not invaded. The tumour readily separated from the brain tissue, revealing considerable destruction of the corpus callosum and the right callosal convolution.

Case 7 (Johns Hopkins Hospital, Baltimore).—Tumour of anterior two-thirds of corpus callosum. Seven months' history of apathy and dullness, poverty of ideas and slowness of thought. Later, headache, with stiffness of the neck, vomiting, giddiness and diplopia. Right peripheral facial palsy. Tendency to fall forwards.

Bessie M., aged 37. Admitted under Dr. Dandy, February 2, 1926. Died, February 24, 1926.

The patient attended the Johns Hopkins Dispensary on February 1, and at this time it was ascertained from her sister that for seven months she had been dull and apathetic, with poverty of ideas and slowness of thought. During this time the patient had begun to suffer from occipital headaches and double vision. In her sister's words, "She cannot seem to think right and is slow in performing her duties around the house." For some time she had had a staggering gait, and when she fell it was almost always forwards on her face. Five months before she had complained of "pins and needles" in both upper limbs.

About three months before admission, she had a period of marked improvement which lasted for some weeks. Her headaches again became worse, she frequently vomited, and for three or four days prior to her admission she was incontinent of urine.

On admission to the hospital the next day, she was found to have bilateral papilloedema and a right peripheral seventh nerve palsy. There was no evidence of involvement of the pyramidal tracts.

Ventriculography was performed and the fluid withdrawn was blood-stained. X-ray pictures, after injecting the ventricles with air, demonstrated clearly a mid-line tumour lying anteriorly. Three days later, Dr. Dandy performed an operation but found an inoperable glioma, and three weeks later the patient died.

At autopsy, a vascular tumour about 2 cm. in diameter was found occupying the anterior two-thirds of the corpus callosum, extending towards the interna capsule and the optic thalamus on the left side. The ventricles were not dilated, but the anterior horns were largely occupied by a greyish tumour mass

growing from the corpus callosum and measuring 4 cm. in transverse diameter and from 2 to 3 cm. vertically. The fornix lay on its lower surface. This growth involved the genu and reached into the superior longitudinal fissure. A small tumour mass occupied the anterior part of the left caudate nucleus.

Here the psychical changes appeared early, when somatic disturbances were slight, and some months before increase of intracranial pressure was evident. Incontinence is a symptom in this and in the following case and we connect it with the psychical condition. The tendency of this patient to fall forwards is worth noting. In a large tumour of this kind it is probably due to backward pressure on the vermis of the cerebellum. A study of cases of corpus callosum tumours in the literature in which this has occurred leads one to the conclusion that it is most commonly met with in tumours of the splenium.

The value of ventriculography in localizing these tumours is well illustrated in the above case.

Case 8 (*Johns Hopkins Hospital, Baltimore*).—*Tumour of the splenium. Early marked psychical changes, forgetfulness, "holes in the memory"; later, mental confusion. Four months' vomiting, headache and papilledema. Diminution of sensibility over the left half of the body. Absence of abdominal reflexes on the left side.*

Claud W., aged 50. Admitted under Dr. Dandy on June 25, 1922. Died, July 12, 1922.

The patient's earliest symptoms were inability to remember and to think clearly, and drowsiness. Some months later his memory had become so bad that he could not remember what had been said to him or statements made by himself a few minutes before. For three months previous to his admission he had suffered from frontal headaches, dimness of vision, and a month before admission from vomiting.

On examination bilateral papilledema was found. The pupils were equal, irregular in outline and reacted sluggishly to light. The visual fields could not be tested owing to the patient's mental state, but on several occasions he stated that he had constant dimness of vision and said he felt as though there was a film over his eyes. There was some sensory loss to cotton wool and pin prick over the entire left half of the body and the abdominal reflexes were absent on the left side. The plantar reflexes were flexor. The Wassermann reaction was negative.

The patient died after decompression, and at autopsy a tumour was found growing from the splenium 2 cm. in transverse diameter, compressing the posterior horn of the right lateral ventricle and extending into the occipital lobe and the optic thalamus on the right side. The fibres of the fornix were entirely replaced by the growth, which also involved the pineal gland. The pyramidal tracts appeared to have entirely escaped injury.

As in Case 5, and Dr. Collier's case, marked failure of memory for recent events led to difficulties in examination and discrepancies in the patient's statements. The psychical changes occurred many months before the onset of signs in the limbs. The drowsiness was probably due to encroachment of the growth on the third ventricle. The pineal gland and the roof of the third ventricle were found to have been destroyed by the neoplasm.

Case 9 (National Hospital, Queen Square, London).—Tumour of the anterior two-thirds of the corpus callosum. Three months' history of mental changes, drowsiness and incontinence. Choreiform movements in the right upper and lower limbs followed by right-sided weakness, and later, bilateral pyramidal signs and quadriplegia. Cerebrospinal fluid clear.

Frances C., aged 37. Admitted under Dr. Buzzard, May 28, 1919. Died, June 7.

The patient was a Pole and could speak very little English. Three months before admission she began to suffer from intense headache and depression. Two months before admission she took to her bed and since then frequently had incontinence and mental confusion. One month before admission her family noticed jerking and writhing movements in the right upper limb.

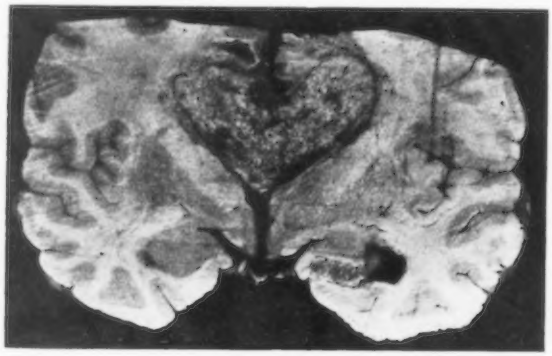

FIG. 3 (*Case* 9).—Coronal section of the brain through the third ventricle to show tumour occupying the body of the corpus callosum, invading the fornix and the lateral ventricles.

On examination the patient was a well-nourished woman, who could be roused to answer questions. Marked echolalia—when told to say "No," she would say "Say no;" and when told to say "Yes," she replied "Say yes." When disturbed there were intense choreiform movements in the limbs and face, more marked on the right side, and there was an exaggerated restlessness and fidgetiness in trying to make her grip or perform an action. Both plantar

responses were extensor. The patient dropped off to sleep during the examination. The optic discs appeared normal.

One week later the choreiform movements had ceased and the patient was more comatose. A right hemiparesis gradually developed. Two days later the left leg had become paralysed and flaccid, and two days later all four limbs were powerless and slightly spastic.

The cerebrospinal fluid was clear, contained 0·04 per cent. of albumin; there were no cells and no excess of globulin. The Wassermann reaction was negative in blood and cerebrospinal fluid.

At autopsy a large tumour was found occupying the genu and anterior two-thirds of the corpus callosum (see fig. 3).

There is little doubt that the incontinence of these patients is of the mental type and is due to defect of attention and apathy. A considerable proportion of cases in the literature have shown drowsiness, an irresistible tendency to sleep and increasing obesity. It is probable that in these cases these symptoms are due to encroachment of the growth on the third ventricle and infundibulum. The descriptions by various authors of the psychical changes are remarkably alike; thus, Bristowe talks of "a stuporous condition, with lethargy and slowness of speech"; Ransom, of "increasing stupor with later hallucinations and bouts of irritability"; Schüpfer, of "lethargy and apathy"; Bruns, of "mental confusion, incontinence and great mental failure in the absence of any marked physical signs." It is to Raymond that we owe our first clear description of these psychical changes. He is the first of the earlier authors to contrast the psychical disturbances of brain tumours generally with those of the corpus callosum. Raymond stressed the early appearance of: (1) Changes in character; (2) dissociation of ideas and lack of continuity in thought; (3) eccentricity of conduct; (4) disturbance of memory, especially for recent events—"holes" in the memory; and (5) grave changes in character and variability of temperament.

This syndrome, to have localizing value, must appear early and in the absence of other somatic disturbances. We agree that this syndrome appears to be the one which is most frequently present in whole or part, but care must be taken to separate changes which may be due to general increase of intracranial pressure. In our experience the disease picture most commonly arises with a depressive condition.

An extremely comprehensive account of the psychical changes in tumours of the corpus callosum has recently been published by Egas Moniz, of Lisbon. The first of his cases, in the absence of all signs of

increased intracranial pressure, showed marked psychical changes. The patient was drowsy but far from being apathetic. He showed diminution of intelligence, memory defect and poverty of ideation. There was deterioration of the moral sense, coprolalia, and loss of interest in his family and friends, recalling the picture of dementia præcox.

This author relates the type of mental change to the age of the patient. He states that in the young a syndrome recalling dementia præcox is common; in middle life the psychical changes simulate those of general paralysis, and in the aged those of senile dementia.

Every psychosis, however, may be simulated, especially the manic-depressive and dementia paralytica. Cases with paranoid symptoms and Korsakoff's psychosis are to be found in the literature. In Levy-Valensi's cases 57 showed apathy or emotional indifference; 17 defect of memory for recent events, sometimes simulating a Korsakoff state; 14 an irresistible tendency to sleep; 7 were disoriented, with a confusional state; 6 had bouts simulating mania, and 3 were definitely melancholic; 4 cases had hallucinations, and 2 delusions of persecution.

III.—*Cases illustrating Early Onset of Epileptiform Convulsions.*

In the cases already recorded fits have occurred during the course of the illness. In Case 3, Jacksonian attacks were noticed on the side in which the weakness was most marked. In Case 5 uncinate fits were observed early in the disease, and in Case 6 the epileptiform convulsions were generalized. In Cases 10 and 11, recorded below, generalized epileptiform convulsions were the earliest symptom and preceded the onset of mental changes and motor weakness, in the first case by six years and in the second case by four years.

Case 10 (*National Hospital, Queen Square, London*).—*Tumour of the genu and forceps anterior. Six years' history of epileptiform convulsions with occasional headache and vomiting, the left pupil enlarging during the attacks. Two months' history of drowsiness, slowness and apathy. Bilateral papilloedema, and later slight left-sided pyramidal signs.*

Stanley A., aged 33. Admitted under Dr. Buzzard, November 5, 1920.

Six years before admission the patient began to suffer from attacks in which he fell suddenly unconscious on his face on the floor. His sister stated that there was no rigidity or jerking of his limbs during the attacks, and that they lasted from ten to fifteen minutes. The attacks were always followed by vomiting and severe vertical headache. There were long intervals between his attacks. In the six years he had had perhaps seven altogether. Two months before admission, having been for a year free from fits, he noticed double vision for distant objects.

On examination he was a stout, fresh-complexioned man. Cerebration was notably slow and there was extreme lethargy, the patient dropping off to sleep constantly during the examination. His attention was poor; at times he was semi-comatose and roused only with difficulty. When roused he appeared intelligent and a good witness, though his reaction time was prolonged. There was great apathy and disinclination to be bothered with the fatigue of examination. His speech, when obtained, was normal, and there was no apraxia. The patient gave inaccurate replies to smelling tests.

Visual acuity in both eyes was $\frac{6}{18}$. The fields were full to rough testing. Papilloedema measured four dioptres in the right disc and five dioptres in the left.

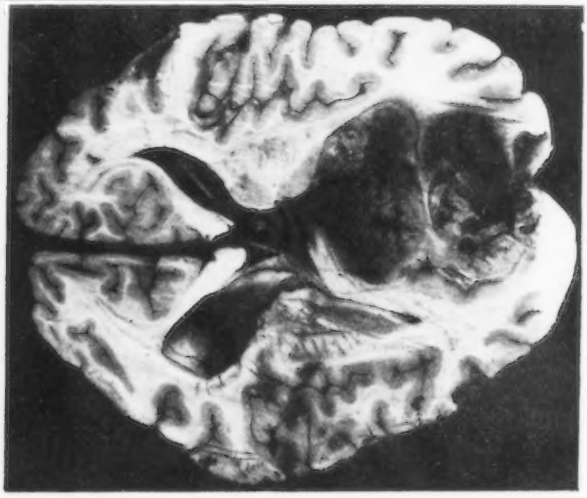

FIG. 4 (*Case* 10).—Sarcoma of the genu of the corpus callosum, exposed from above. This extremely vascular and hæmorrhagic growth had produced internal hydrocephalus by obstruction of the foramina of Monro.

The surfaces of the discs exhibited a greyish speckled appearance, there were no hæmorrhages and no macular disturbance. Convergence was poor, especially of the left eye, and there was weakness of the right external rectus with fine nystagmus of the left eye on looking to the extreme right. Taste was normal on the tongue; there was marked tremor of the protruded tongue. There was slight weakness of the left lower face on voluntary and emotional movement.

A detailed examination of the motor system revealed no weakness, ataxia, or involuntary movement. Tone was slightly diminished in the left arm and leg. All the arm-jerks were absent; the knee-jerks were sluggish; the left ankle-jerk was brisker than the right; the right plantar was flexor, the left definitely extensor; the abdominal reflexes could not be elicited on the left side. There was no sphincter disturbance.

Four days after admission the patient was seen in an attack: the right pupil was smaller than the left, the left arm was extended and pronated, and there was opisthotonos. Patient had several fits after this, in all of them the left upper limb assuming the same position, the right pupil being smaller than the left.

That evening a right-sided decompression was performed. Five hours later the patient died.

At autopsy, a large tumour was found occupying the genu of the corpus callosum in the region of the forceps anterior. There was an area of thrombosis and softening in the distribution of the left anterior cerebral artery. The growth had extended into the right lateral ventricle and there was considerable dilatation of the posterior and descending horns, with compression of the right internal capsule (see fig. 4).

Case 11 (*National Hospital, Queen Square, London*).—*Tumour of splenium, invading the right optic thalamus. Four years' history of epileptiform convulsions with visual aurœ. One month ago onset of mental change—apathy and impairment of memory for recent and remote events. Great lethargy, and later, delusions of persecution. Bilateral papilloedema. Palilalia. Unequal pupils and double vision. Slight progressive left-sided weakness with sensory loss. Sudden death after a severe attack of headache.*

Elizabeth H., aged 37. Admitted under Dr. Buzzard, August 10, 1894.

Four years ago the patient began to suffer from epileptic fits. She stated that her attacks were preceded by a sudden flash of bright light, or a sensation of darkness that seemed to come over her from the left side of her head. This was accompanied by a sensation of "fearful dread." An eye-witness stated that she gave two screams—the first, a scream of "It is coming"—the second, a hollow cry, coincident with her fall and loss of consciousness.

In the attack the head and eyes turned to the left, and later there was bilateral jerking of the limbs. On regaining her senses the patient moaned greatly as if in pain, and if spoken to would go off again into another convulsion. After the attack patient was said to be dazed and to suffer from headache. During the attack patient usually bit her tongue. There was no history of automatic acts following the seizures.

At first she used to have several attacks each day. Afterwards the fits occurred about once a week. Before each fit she was conscious of a light revolving on the left side and everything around becoming quite dark. Sometimes she was conscious of what looked like the shadow of a person on her left side, but this feeling was never followed by convulsion.

One month before admission patient had a very severe attack, and after that her brother noticed extreme lethargy day and night, great apathy and memory defect. Her speech, too, had become slower. Patient herself stated that occasionally she saw double.

The patient gave a history of previous good health. The catamenia had always been regular. The family history showed that one sister suffered from

fits, an uncle had committed suicide and an aunt had died in an asylum. Her mother and one sister had suffered from consumption.

On examination the patient was a well-nourished woman of good colour. Her facial expression was placid, almost vacant, and cerebration seemed slowed down to a remarkable extent. She seemed to have lost interest in everything and wished only to be left alone, untroubled. Her memory was impaired for recent and remote events. She could not remember where she was, and thought that she was going to be ill and treated in some way. She did not recognize her relatives and was constantly dropping off to sleep. Her speech was slow and sibilant, and she frequently repeated words and syllables. She never complained of severe headache. Vision in the right eye was $\frac{6}{5}$ and in the left eye $\frac{6}{12}$. Both optic discs were blurred with three dioptres of swelling in the right disc and five dioptres of swelling in the left disc. There were no retinal hæmorrhages. The fields of vision were full to rough testing.

A detailed examination of taste and smell revealed no defect of smell but a general blunting of taste. The right pupil was smaller than the left and there was slight left lower facial weakness. There was no motor weakness of the limbs; the tendon reflexes were brisk and equal; the upper and lower abdominal reflexes were brisk, and there was no incontinence. Some blunting to cotton-wool and pin prick was noticed on the left side of the trunk, limbs, and face, and sense of position was impaired in the fingers of the left hand.

Three months later the patient's mental state continued to deteriorate. She was continually getting out of bed, resisting, and talking about plots against her, asking often for a policeman or a clergyman. She accused the house physician of being a great villain who plotted against her, and did not recognize either her doctor or her nurses. She took a long time to comprehend what was said to her.

Later, the patient became mentally clear and the swelling of her discs subsided. Two months later she again became dull mentally, lethargic and apathetic. Delusions of persecution again became evident. She thought that her food was being poisoned, and again that she was in an asylum. There was no apraxia or aphasia. The drowsiness increased and slight left-sided weakness became evident. The temperature rose to 102° F., and she developed a basal pneumonia, from which she recovered.

Ten months after admission the patient was getting up for some hours each day, showing definite left-sided weakness. Fourteen months after admission she died suddenly after a severe attack of headache.

At autopsy a tumour of the splenium was found, invading the right optic thalamus.

The visual auræ in this case would appear to be due to the extension of the growth towards the occipital cortex. The psychical changes are worthy of note. In the early stages drowsiness and vacant expression were observed, with slowness of thought, speech, and action. This is the only one of our cases in which definite delusions of persecution

arose. The remissions in the mental state, which were first emphasized by Ransom, are typified in the later history of this patient.

Case 12 (*Johns Hopkins Hospital, Baltimore*).—*Tumour of posterior two-thirds of corpus callosum. Fractured skull seven months before admission. Since then frequent epileptiform convulsions. Drowsiness, failure of memory and apathy. Admitted comatose. Slight left hemiplegic weakness.*

James B., aged 59. Admitted under Dr. Dandy January 21, 1927. Died January 30.

Seven months before admission patient was hit on the head by a falling tree and sustained a fractured skull, but was able after a week to return to his farm work. After this accident he suffered from frequent generalized epileptiform convulsions, and it was noticed that his mentality was becoming duller, his memory more defective, and slowness and poverty of thought became marked. Three weeks before admission he went to bed with headaches and drowsiness.

On examination there was slight left hemiplegic weakness. The fundi were normal. The day after admission ventricular puncture was performed, and showed that both lateral ventricles were dilated. Ventriculography showed the dilatation mostly in the anterior horn of the right ventricle. The skull showed evidences of old fracture.

At autopsy the ventricles were found to be dilated and to contain blood-stained fluid and clot. A soft, gelatinous tumour grew from the middle and posterior third of the corpus callosum into the ventricles, destroying the body of the corpus callosum and the splenium.

It is worthy of mention that in this case and in Case 14 there is a history of fracture of the skull. It is commonly taught that trauma plays no rôle in production of gliomata, but Cushing has suggested that it may do so in sarcomata and endotheliomata. A history of head injury is relatively frequently obtained in patients with cerebral tumour, and the explanation of it may be that the impairment of mental alertness, as the result of the growth, renders the patient incapable of avoiding accidents.

Case 13 (*National Hospital, Queen Square, London*).—*Tumour of the middle of the corpus callosum and the right island of Reil. Gradual onset of right hemiparesis, weakness spreading to the left side, with memory defect, slowness of cerebration and depression. Fits. Tremor of left arm and leg. Pleocytosis of* 79 *cells per c.mm. in the cerebrospinal fluid.*

William T., aged 52. Admitted under Dr. Taylor, August 24, 1919.

Five weeks before admission the patient, who was left-handed, began to have "faints" at his work, and his wife noticed the gradual onset of weakness and shaking in the right arm and leg. The right-sided weakness became progressively worse, and six days before admission the left arm and leg began to

be similarly affected. During the eight days preceding his admission to hospital, the patient had three epileptiform convulsions with loss of consciousness, each lasting only a few minutes. He complained, on admission, of severe frontal headache.

On examination the patient was apathetic and slow of speech and cerebration, but there was no aphasia. He complained that "his memory had gone" and that he felt intensely depressed. Both optic discs were blurred but there was no appreciable swelling.

On testing with cotton-wool and pin prick the patient missed occasional touches on the right half of the trunk and right limbs, and in the right upper limb there was considerable loss of the sense of position. There was weakness of both upper limbs, greater in the right. The right lower limb was flaccid and feeble, voluntary power remained only in the quadriceps and adductors. The tendon reflexes were elicited briskly. The knee-jerks were brisker on the right side than on the left. Right ankle clonus was present. The right plantar response was extensor, the left flexor and the abdominal reflexes were absent on the right side and present on the left.

One week later the patient, although conscious, stated that he felt dazed and depressed. An occasional tremor was seen in the left upper and lower limbs. Both plantar responses were definitely extensor.

Cerebrospinal fluid.—Clear, colourless, 79 cells per c.mm., large and small mononuclears and phagocytes; albumin 0·05 per cent; chlorides 0·73 per cent; good reduction of Fehling; Wassermann reaction negative.

The temperature rose to 105° F., and the patient became comatose and died on September 5, 1919.

At autopsy a tumour was found occupying the middle of the corpus callosum and running outwards on the right side to the island of Reil.

In this case the attacks were simple, slight losses of consciousness, without convulsions. Here again, but for the result of the examination of the cerebrospinal fluid, a diagnosis of cerebral arteriosclerosis might be made.

IV.—*Tremor and Choreiform Movements.*

Cases 2, 4, 5, 6, and 13 presented tremor or tremulousness in one or more limbs. Case 9 had a right hemichorea. In Case 5 a tremor of the right upper limb was associated with a statuesque gait, rigidity and Parkinsonian attitude. This has been noted also by Guillain in a case published in the *Annales de Médecine*, in 1922, and by Bristowe in one of his four cases published in 1884. As in Case 6 of our series, a pyramidal hemiplegia on the one side may be associated with tremor in the contralateral limbs. Fourteen of Levy-Valensi's cases had involuntary movements. In eleven of these cases there was true rhythmic

" tremblement," in two cases there were choreiform movements, and in one case successive clonic jerkings of all four limbs.

V.—*Cerebrospinal Fluid.*

In seven of our cases an examination of the cerebro-spinal fluid was made, and in two the ventricular fluid was examined. In three of these cases only were the findings entirely negative. Four of the cases showed xanthochromia, increase of total protein (0·06 to 0·3 per cent.), with pleocytosis varying from 10 to 79 cells per c.mm. These findings, in a series of tumours selected because of their strict confinement to the corpus callosum, seem to be of very great importance.

The examination of cerebrospinal fluid in the majority of cerebral tumours gives negative results. Alterations in the cerebrospinal fluid in cerebral tumour appear to take place only when the tumour itself is actually in relation to the cerebrospinal fluid, either in the ventricles or basal cisterns. It can be easily understood that from their situation and vascularity, tumours of the corpus callosum are likely to give rise to direct passage of blood protein and tumour cells into the cerebrospinal fluid. Meningeal or cortical tumours are usually firm, avascular endotheliomata, and they rarely cause any alteration in the fluid in spite of their size. In the multitudinous case reports extant on tumours of the corpus callosum, the records of cerebrospinal fluid examination are incomplete or altogether wanting and, so far as we can ascertain, no other writers have emphasized these changes in the cerebrospinal fluid.

VI.—*Other Symptoms.*

In seven of our fourteen cases the pupils were unequal. In one case the inequality was noticed only during epileptiform fits. In six of our cases some degree of aphasia was present, and in these cases the predominating weakness was always on the right side. In Case 13, in which the predominating weakness was right-sided, aphasia was absent, but here the patient was left-handed. In all cases in which the predominating weakness was left-sided there was no aphasia whatever. In the aphasic cases perseveration was marked, and in Case 9 the patient had echolalia.

VII.—*General Symptomatology.*

Most authors are in agreement with Bristowe that in tumours of the corpus callosum the general signs of increased intracranial pressure

are often absent or slight. If this applies to headache, vomiting and giddiness, it does not, however, refer to papillœdema, which has been found by Balduzzi in 54 per cent. of a series of 107 cases. It was present in nine of our fourteen cases. The percentage is probably higher than Balduzzi states, as in all of his cases a detailed fundus examination was not made. The changes appear to be constantly bilateral. We agree with Raymond, who has stated that headache begins early and advances *pari passu* with the psychical changes. Vomiting is much rarer, appears always to be accompanied by headache, and is never an isolated symptom.

Case 14 (*Johns Hopkins Hospital, Baltimore*).—*Tumour of body of the corpus callosum. Fractured base twenty months before admission, resulting in right-sided total deafness, tinnitus, vertigo and headaches. Temporary periods of amaurosis. Gross papillœdema.*

Benjamin S., aged 32. Admitted to Johns Hopkins Hospital November 9, 1912. Died November 17.

Twenty months before admission the patient was struck in the right parietal region by the limb of a tree and was rendered unconscious. Subsequently X-ray demonstrated a fracture of the base of the skull. After this he began to have frontal headaches lasting for about half an hour, accompanied by delirium, and he had attacks of vertigo and vomiting, often three times a day. It is probable that these attacks were connected with his head injury.

Ten months before admission his headaches became much more severe and he developed double vision.

On examination the swelling of the right disc measured seven dioptres. There was consecutive atrophy and total loss of vision in the right eye. The swelling of the left disc was rather less and the fingers could be counted at one metre with the left eye. The left pupil reacted feebly to the light; the right was fixed. It was noted that the patient was totally deaf in the right ear and there was some weakness of the right side of the face. He complained of a feeling of numbness over the distribution of the second division of the right fifth nerve. His gait was staggering and ankle clonus was noted in the right side.

Cerebellar exploratory operation was performed by Dr. Hener and proved negative.

At autopsy, a large tumour about the size of an orange was found, occupying the body of the corpus callosum and extending into both hemispheres, compressing the lateral ventricles and giving them a Y-shape.

VIII.—*Radiological Findings.*

Schaffer has recorded a case in which the tumour extended towards the third ventricle, causing obesity of the pituitary type, with erosion

of the posterior clinoid processes of the pituitary fossa. Occasionally calcified masses in the neoplasm of the corpus callosum may be visible in the X-ray.

Although we have had but little opportunity for making observations, it would appear that ventriculography has a considerable field in the diagnosis of these median tumours. In Case 7 it established the site of the tumour. Ventricular distortion is an almost constant post-mortem finding and the neoplasm frequently involves the septum lucidum.

Localization within the Corpus Callosum.

The diagnosis of tumour of the corpus callosum has been in the past so largely a matter of conjecture, that any attempt to formulate localization of the growth to particular regions of the corpus callosum would appear to be almost too idealistic. We believe that this can be done only in rare instances, in which the clinical picture is distinctive and the "neighbourhood" symptoms well marked. In 1899, however, Schüpfer attempted to draw up criteria distinguishing the portion of the corpus callosum which was invaded by the growth. He stated that tumours of the genu were characterized by: (1) The early development of psychical in relation to motor disturbances; (2) isolated, or early unilateral or bilateral central facial palsy; (3) a tendency of the head to rotate towards the paralysed side; (4) rigidity of the neck muscles; (5) greater paresis in the arms than in the legs; (6) ataxia. Tumours of the middle portion were said to develop a paresis of both upper and lower limbs, progressing to a total paralysis. Tumours of the splenium were marked by: (1) onset of paresis in the lower limbs before the upper limbs; (2) absence of facial paralysis; and (3) a weak, uncertain and ataxic gait.

We have been unable to confirm these observations.

Differential Diagnosis.

In making the diagnosis of a tumour of the corpus callosum we have to consider, *firstly*, the differentiation from pathological cerebral conditions other than tumour, and *secondly*, the differential diagnosis from tumours in other regions of the brain. The condition most closely simulating the syndrome presented by tumours of the corpus callosum is cerebral arteriosclerosis. The psychical changes, bilateral pyramidal signs, tremor and other involuntary movements may be closely simulated, and, as we have already emphasized, in many cases of corpus callosum tumours the general symptoms of increased intracranial pressure may

be absent. Many cases of cerebral tumour show concomitant arteriosclerotic changes, and it must not rashly be concluded that epileptiform convulsions are the result of cerebral arterial changes, or of a mild degree of uræmia, even if this is shown to be present by biochemical examinations. In making the differential diagnosis between the two conditions we would emphasize the importance of the finding of changes in the cerebrospinal fluid, either xanthochromia or pleocytosis, as being strong evidence of tumour. Such findings are rare in ingravescent cerebral arteriosclerosis and occur only in subarachnoid hæmorrhage, or after thrombosis of the middle cerebral artery in the Sylvian fissure, both of which conditions have easily differentiated clinical pictures.

The differential diagnosis from *dementia paralytica* can usually be made by the examination of the blood and cerebrospinal fluid.

The distinction of tumour of the corpus callosum from *cerebral tumours elsewhere* may cause difficulty. Cases with the characteristic early apathy or drowsiness, with an ingravescent hemiplegia, with pyramidal signs on the opposite side, with epileptiform convulsions, tremor, yellow cerebrospinal fluid and perhaps unequal pupils, can be localized with some degree of confidence in the corpus callosum. Other cases, in which the signs are less definite, may be confounded with frontal or temporal tumour. The presence of left-sided motor apraxia is a positive sign of great localizing value when it is present, but we believe this symptom is present only in about 10 per cent. of cases. In all instances where there is doubt ventriculography should be considered as a possible means of throwing light on the localization.

The diagnosis *from multiple tumours of the brain* is perhaps most difficult of all, as here we can rely only on the early appearance of the characteristic mental changes.

Pathology.

Balduzzi has analysed 76 cases in which a histological examination had been made. Glioma is by far the commonest growth of the corpus callosum, and was found in 27 of his cases. In 18 cases sarcoma was found, and in 10 cases gliosarcoma. All other types of growth are relatively rare. Myxosarcoma, carcinoma and lipoma may be met with as primary growths in the corpus callosum. Gummata were found twice in Balduzzi's 76 cases.

The occurrence of lipomata in the corpus callosum has been noted from time to time. Leichtenstern, in 1887, showed the brain of a woman who had died of pneumonia, in which a lipoma, extending from

the genu to the splenium, was discovered as a chance finding. Virchow had called attention to the fact that at the genu and in the neighbourhood of the anterior pillars of the fornix fat may be found normally. Rokitansky described a lipoma the size of a pea in the ependyma of the corpus callosum. Similar cases have been described by Pagliese (1895), Steigert (1902), Würth (1903), and others.

Gliomatous tumours of the corpus callosum do not tend to grow along the striæ. Those of the genu extend into the frontal poles, those of the middle portion into the corpus striatum and downwards towards the third ventricle. It may frequently be noticed that growth into the lateral ventricle is limited by the ependyma of that structure. This was a marked feature in Cases 2, 5 and 10 of our series. Tumours of the splenium tend to extend into the optic thalamus and along the optic radiations, pushing into the body and posterior horns of the lateral ventricles.

Some distortion of the internal capsule in whole or part is almost constantly found, and the lateral ventricles are rarely symmetrical. Unilateral hydrocephalus may be met with from blockage of the foramen of Monro, and in tumours of the splenium obstructive internal hydrocephalus occurs from blockage of the aqueduct of Sylvius. Some degree of internal hydrocephalus may arise, apart from ventricular obstruction, presumably due to deflection of the falx, with consequent compression of the great vein of Galen, thus inducing an excessive production of cerebrospinal fluid.

Thromboses in the distribution of the anterior cerebral artery are met with very frequently. It will be recalled that the main branch of this artery, after giving off the calloso-marginal artery, courses backwards along the indusium of the corpus callosum, supplying the anterior 7/8 of the corpus callosum and the centrum ovale in the region of the head of the caudate nucleus. The two halves of the choroid plexus may be widely separated by growths of the splenium, and this structure may be compressed so that it lies in apposition to the lateral walls of the body of the ventricles.

In Levy-Valensi's series of 74 cases, the growth was located 28 times in the genu, 19 times in the splenium, and 8 times in the body of the corpus callosum. In 19 of these cases the whole of the corpus callosum was involved. In a large series collected by Bruns, growths of the corpus callosum were found three times more frequently in men than in women, and most frequently between the ages of 30 and 40 years.

Treatment.

It is possible that were these growths diagnosed early they might be amenable to surgical intervention. Third ventricle tumours have been approached by cutting the corpus callosum sagittally, and we believe that some of these cases have recovered without disability from the partial destruction of the corpus callosum entailed by the operation.

Short of surgical removal, it is possible that treatment of these tumours by radium or by deep X-rays may be attended with some success. Decompression is an essential preliminary to relieve the increased intracranial pressure, to allow for œdema occurring in the neighbourhood of the growth during treatment, and to provide a window in the bone for irradiation. It is known that while both the grey and white matter is highly radio-resistant, cerebral neoplasms, especially gliomata, are sensitive to gamma-rays and to X-rays. Successes in the treatment of deep tumours of nervous tissue have been reported recently where the method used was preliminary implantation of radium needles, suitably screened, in the growth, and subsequent treatment for two to three weeks by daily application of a Columbia paste helmet in which radium needles of suitable dosage are embedded.

Treatment of these tumours by deep X-rays may be attended with some success. Here we would emphasize again the value of preliminary decompression. The central localization renders the growths easy of access by the rays and, owing to the peculiar position of these tumours, no severe complications may be feared from this form of treatment.

Bibliography.

[1] Ayala, G. "Contributo allo studio dei tumori del Corpo calloso," *Riv. di Patol. nerv.*, 1915, **20**, 449.

[2] Balduzzi, O. "Die Tumoren des Corpus Callosum," *Arch. f. Psychiatr. u. Nervenkeill.*, 1927, **79**, 1.

[3] Bechterew, W. v. "Die Leitungsbahnen im Gehirn und Rückenmark," Leipzig, 1899.

[4] Beevor, C. E. "On the Course of the Fibres of the Cingulum and the Posterior Parts of the Corpus Callosum and Fornix in the Marmoset Monkey," *Phil. Trans. Roy. Soc. Lond.*, 1892, **182**, 135.

[5] Bianchi and D'Abundo. "Le degeneraz. sperim., etc.," *La Psichiatria*, 1886.

[6] Bykoff. Abstract in *Zentralblatt f. d. ges. Neurol. u. Psychiatr.*, 1924-5, **39**, 199.

[7] Bristowe, J. S. "Tumour of the Corpus Callosum," *Brain*, 1884, **7**, 315.

[8] Brown-Sequard, C. E. "Sur l'existence dans chacun des hémisphères cérébraux de deux séries de fibres capables d'agir sur les deux moitiés du corps, soit pour y produire des mouvements, soit pour déterminer des phénomènes inhibitoires," *Compt. rend. Soc. de Biol.*, 1887, Ser. 8, **4**, 261.

[9] Bruce, A. "Absence of Corpus Callosum in the Human Brain, with a Description of a New Case," *Brain*, 1890, **12**, 171.

[10] Bruns, L. "Ueber Tumoren des Balkens," *Berl. klin. Wochenschr.*, 1886, **23**, 340.

[11] Chopart, F. "Mémoire sur les lésions de la tête, par contre-coup," Paris, 1771.
[12] Corner, G. W. "Anatomists in Search of the Soul," *Ann. Med. Hist.*, 1919, **2**, 1.
[13] Dejerine, J. J. "Anatomie des centres nerveux," Paris, 1901. **2**.
[14] Dotto and Pusateri. "Sul decorso delle fibre del corpo calloso e dello psalterium," Pisani, Palermo, 1897, **18**.
[15] Eichler, G. "Ein Fall von Balkenmangel im menschlichen Gehirn," *Arch. f. Psychiatr.*, 1878, **8**, 355.
[16] Ferrier, D. "Experiments on the Brain of Monkeys—No. 1." *Proc. Roy. Soc. Lond.*, 1874-1875, **23**, 409.
[17] Flourens, J. P. M. "Recherches expérimentales sur les propriétés et les fonctions du système nerveux," édit. 2, Paris, 1842, p. 21.
[18] Foix and Hillemand. "Les syndrômes de l'artère cérébrale antérieure," *L'Encéphale*, 1925, **20**, 209.
[19] Foville, A. "Traité complet de l'anatomie de la physiologie, et de la pathologie du système nerveux," Paris, 1844.
[20] Gand. Quoted by Mingazzini, "Der Balken," p. 169.
[21] Garrison, F. H. "History of Medicine," 3rd edition, 1921.
[22] Gowers. "Diseases of the Nervous System," 2nd edition, 1893, **2**, 314.
[23] Greenfield and Carmichael. "The Cerebrospinal Fluid in Clinical Diagnosis," London, 1925, p. 187.
[24] Guillain, G. "Sur un cas de tumeur du splénium." *Rev. Neurol.*, 1922, **29**, 23-27.
[25] *Idem. Annales de Méd.*, 1922, **11**, 33.
[26] Haeser, H. "Lehrbuch der Geschichte der Medicin," 3rd edition, Jena, 1875.
[27] Hamilton, D. J. "On the Corpus Callosum in the Adult Human Brain," *Journ. Anat. and Physiol.*, 1884-1885, **19**, 385.
[28] *Idem.* "On the Corpus Callosum in the Embryo," *Brain*, 1885-1886, **8**, 145.
[29] Hartmann, F., jun., and Trendelenburg. "Zur Frage der Bewegungsstörungen nach Balkendurchtrennung an der Katze und am Affen," *Zeitschr. f. d. ges. Exper. Med.*, 1927, **54**.
[30] Henry, M. "Dissection of a Brain, in which the Corpus Callosum, Fornix and Septum Lucidum were Imperfectly Developed," *Medico-Chirurg. Trans. Lond.*, 1848, **31**, 239.
[31] Henschen, S. E. "Pathologie des Gehirns," 2, 415.
[32] Huddleson. "Ein Fall von Balkenmangel mit Lipomentwicklung im Defekt," *Zeitschr. f. d. ges. Neur. u. Psychiatr.*, 1928, **113**, 177.
[33] Kaufmann, E. "Ueber Mangel des Balkens im menschlichen Gehirn," *Arch. f. Psychiatr.*, 1887, **18**, 769, and 1888, **19**, 229.
[34] Koranyi, A. "Ueber die Folgen der Durchschneidung des Hirnbalkens," *Pflüger's Arch. f. Physiol.*, 1890, **47**, 35.
[35] Lafora, G. R., and Prados y Such. "Experimentalversuche über die Function des Gehirnbalkens," *Zeitschr. f. d. ges. Neurol. u. Psychiatr.*, 1923, **84**, 617-641.
[36] Lancisi, J. M. "Dissertatio Altera. De sede Cogitantis Animae," T. 2, Geneva, 1718, p. 302.
[37] La Peyronie, F. G. "Observations par lesquelles on tâche de découvrir la partie du cerveau où l'âme exerce ses fonctions," *Acad. Royale des Sciences, Paris. Mémoires de Mathématique et de Physique.* 1741, p. 199.
[38] *Idem. Mém. et Journal de Travaux*, 1709, p. 609.
[39] Leichtenstern. "Ein Fall von Balkentumor," *Deutsch. med. Wochenschr.*, 1887, **13**, 1128.
[40] Leuret, F., and Gratiolet, L. P. "Anatomie comparée du système nerveux," 1839-57, **2**, 57.
[41] Levy-Valensi, J. "Le corps calleux (étude anatomique, physiologique et clinique)," *Thèse de Paris*, 1910.
[42] *Idem.* "Physiologie du corps calleux," *Presse Méd.*, 1911, **19**, 72.
[43] Lewandowski. "Die Funktionen des zentralen Nervensystems," Jena: Fischer, 1907.

[44] LIEPMANN, H. "Die linke Hemisphäre und das Handeln," *Münch. med. Wochenschr.*, 1905, **52**, 2322, 2375.

[45] *Idem.* "Ueber die Funktionen des Balkens beim Handeln und die Beziehungen von Aphasie und Apraxie zur Intelligenz," *Med. Klinik*, 1907, **3**, 725, 765.

[46] MAGENDIE, F. "Leçons sur les fonctions et les maladies du système nerveux," 1841, **1**, 181.

[47] MALIVERNI. "Absence de corps calleux, de septum lucidum et de la circonvolution du corps calleux dans un cerveau," *Gaz. Méd. de Paris*, 1875, 4th Series, **4**, 33.

[48] MARAT, J. P. "A Philosophical Essay on Man," London, 1773.

[49] MELLUS, E. L. "Bilateral Relations of the Cerebral Cortex," *Johns Hopkins Hosp. Bull.*, 1904, **12**, 108.

[50] MEYNERT, T. "Neue Studien über die Associationsbundel des Hirnmantel," *Sitzungsb. Akad. Wissensch. in Wien*, 1892, **101**, 3, 361.

[51] MINGAZZINI, G. "Ueber die Beziehungen zwischen den Balken und den lentikulären Fasern und der inneren Kapsel," *Deutsch. Zeitschr. f. Nervenheilk.*, 1926, **94**, 168.

[51A] *Idem.* "Der Balken," Berlin, 1922.

[52] MONIZ, E. "Les tumeurs du corps calleux," *L'Encéphale*, 1927, **22**, 514.

[53] MORGAGNI, J. B. "Opera Valsalvae (Epistolas additit. duodeviginti)," Venetiis, 1740, 494.

[54] MOTT, F. W. "Report on Bilaterally Associated Movements, and on the Functional Relations of the Corpus Callosum to the Motor Cortex," *Brit. Med. Journ.*, 1890, **1**, 1124.

[55] MOTT, F. W., and SCHAFER, E. A. "On Movements resulting from Faradic Excitation of the Corpus Callosum in Monkeys," *Brain*, 1890, **13**, 174.

[56] MURATOW, W. "Secundäre Degeneration nach Durchschneidung des Corpus Callosum," *Neurolog. Centralbl.*, 1893, **12**, 316, 714.

[57] PAVLOV. "Conditioned Reflexes," ANREP's Translation, Oxford, 1927, 150-352.

[58] PERRAULT, C. and P. "Œuvres diverses de physique et de mécanique" Leide, 1721, **2**, 403.

[59] PLATER, F. "Observationum," Bâle, 1614, **1**, 13.

[60] PRESTON, C. "An Account of a Child Born Alive without a Brain and the Observables in it on Dissection," *Philosophical Trans. Lond.*, 1695-97, **19**, 457.

[61] RANSOM. "On Tumours of the Corpus Callosum," *Brain*, 1895, **18**, 531.

[62] RAYMOND. "Tumeur du Corps calleux," *Journ. d. Méd. intern.*, 1906, **10**, 268.

[63] REIL, J. C. "Mangel des mittleren und freyen Theils des Balkens im Menschengehirn," *Arch. f. Physiol.*, 1812, **11**, 341.

[64] ROKITANSKY. See references MINGAZZINI—"Der Balken," p. 200.

[65] SAUCEROTTE, N. "Mélanges de Chirurgie," Paris, 1801, p. 290.

[66] *Idem.* "Mémoire sur les contrecoups dans les lésions de la tête," *Mém. pour les Prix de l'Acad. Roy. de Chirurgie*, Paris, 1819, **4**, 334.

[67] SCHRÖDER, P. "Das fronto-occipitale Associationsbündel," *Monatschr. f. Psychiatr.*, 1901, **9**, 81.

[68] SCHUPFER. "Sui tumori del corpo calloso," *Riv. sper. di Fren.*, 1899, **25**, 86; 283.

[69] SHERRINGTON, C. S. "On Nerve-tracts Degenerating secondarily to Lesions of the Cortex Cerebri," *Journ. of Physiol.*, 1889, **10**, 429.

[70] SPRENGEL, K. "Histoire de la médecine," Paris, 1815-20.

[71] STERN. "Die psychischen Störungen," *Arch. f. Psychiatr.*, 1914, **54**, 663.

[72] UGOLOTTI, F. "Contribuzione allo studio delle vie piramidali nell' uomo," *Riv. sper. di Fren.*, 1901, **27**, 38.

[73] *Idem.* "Sulle vie piramidali dell' uomo," *ibid.*, 1906, **32**, 776.

[74] VAN VALKENBURG, C. T. "Experimental and Pathologico-anatomical Researches on the Corpus Callosum," *Brain*, 1913-14, **36**, 119.

[75] VILLAVERDE. "Beitrag zur Entwicklungsgeschichte des Balkens," *Schweiz. Arch. f. Neurol. u. Psychiat.*, 1919, **4**, 45.

[76] Vieussens, R. "Nevrographia," 1685, 123.
[77] Steiger, A. de. "Two Cases of Lipoma of the Brain," *Journ. Ment. Science*, 1902, **48**, 64.
[78] Wepfer, J. J. "Observationes anatomical ex cadaveribus eorum, quos sustulit apoplexia," 1675, p. 392.
[79] Willis, T. "Cerebri anatome," Lond., 1664.
[80] Wilson, Kinnier. "Contribution to the Study of Apraxia," *Brain*, 1908, **31**, 164-216.
[81] Würth. "Ein Beitrag zur Histologie und Symptomatologie der Balkentumoren," *Arch. f. Psychiatr.*, 1903, **36**, 651.
[82] Wysocki and Zbyszewski. "Nouvelles recherches sur l'influence réciproque des hémisphères cérébraux," *Compt. rend. Soc. de Biol. de Paris*, 1925, **93**, 1629-1631.
[83] Zinn, J. G. "Dissertation inauguralis," Göttingen, 1749.

SKIN REACTIONS IN A CASE OF CERVICAL SYMPATHETIC PARALYSIS, WITH A NOTE ON THEIR PRACTICAL APPLICATION TO NEUROLOGY.[1]

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THE skin is innervated by two sets of nerve-fibres, the sensory and the sympathetic. Each has its definite function, and each, at its commencement, takes a different path to reach the skin: the ganglia and the cells lie in different situations and can be damaged separately. The general effects of destruction of each type of nerve are well known. When a sensory nerve is cut or damaged, sensation is lost over the area of skin supplied by that nerve. Sometimes, however, it is difficult to decide where the nerve is damaged; the sensory loss may be due to injury of the nerve, the ganglion or the spinal cord. When a sympathetic nerve is damaged, vaso-dilatation occurs in the area supplied, the pilo-motor spinal reflex is lost and the secretion of sweat is arrested; but again it is not always easy to locate the lesion, which may be in the peripheral part of the sympathetic system, in the ganglion, or central to this. In the case of the sensory nerves the recognized tests are insufficient to show whether the peripheral fibres are degenerate or not; for the sympathetic nerves, this can be determined only by administration of pilocarpine. Recently, however, two simple tests have been made available through the work of Sir Thomas Lewis, Ronald T. Grant and other collaborators [1] [2] on certain reactions of the human skin; these tests should be of value in neurological diagnosis, since they show clearly whether the peripheral nerve-fibres, sensory and sympathetic, are intact or degenerated.

Sensory nerve test.—It has been shown [2] that, when normal skin is injured in any way, for example, by mechanical, thermal or chemical means, it reacts in a definite manner; a triple response of the blood-vessels occurs. At the site of injury a local red spot appears (local vaso-dilatation) followed by whealing (local œdema); around the wheal is a

[1] Work undertaken on behalf of the Medical Research Council.

flare (reflex arteriolar flare). It is this flare that is of interest in nerve lesions. In normal skin the flare appears in about fifteen to thirty seconds after the injury as a pale red flush, which gradually increases in intensity and spreads outwards. At its height it is bright scarlet in colour and extends for about 1 to 3 cm. round the injury and has an ill-defined crenated edge. While the local dilatation and increased permeability of the minute vessels giving rise to the local red spot and the wheal are entirely independent of the nervous system, the arteriolar dilatation giving rise to the flare is dependent on a local axon reflex; if the sensory nerve-fibres are degenerated, the flare fails to appear after injuring the skin. Contrary to Müller's view [5] that the flare depends upon the integrity of the spinal reflex arc, Lewis and his co-workers [2] [3] have shown that the flare is not affected by fresh peripheral nerve section, but is abolished after degeneration (recent or remote) of the sensory nerve-fibres; the flare fails to appear from about the sixth day onwards after nerve section. It follows, therefore, that in the case of a patient presenting anæsthesia of more than a week's duration, if a flare appears on the anæsthetic skin after injury, it may be concluded that the peripheral sensory nerve-fibres are intact and that the anæsthesia is either due to a lesion central to the dorsal root ganglion or is hysterical in origin. If the flare fails to appear on anæsthetic skin, it may be concluded definitely that the peripheral sensory nerve-fibres are degenerated.

For carrying out the test, a needle scratch forms a suitable injury. In cases where the flare is not conspicuous on the skin of a limb, it can be displayed readily by first congesting the veins of the part to render the skin cyanotic; then, after injury, the flare appears bright red on a purple background, as a result of the increased blood-flow through the dilated arterioles.

Sympathetic nerve test.—It is well known that erection of the hairs may be produced on the human skin by means of a reflex through the central nervous system; the application of a piece of ice or various other appropriate stimuli to the skin over the spine causes a generalized erection of the hairs, especially if the body is uncovered in a cool room. Failure of goose-skin to appear on a part indicates interruption of the reflex arc, but does not show whether the peripheral sympathetic fibres are degenerate or not. It is also known that if the skin is sharply struck with a ruler, goose-skin appears over the exact area of stimulation; this is a direct response of the pilomotor muscles and occurs even when the peripheral nerves are degenerate. Lewis and

Marvin [4] have recently shown that if the skin is stimulated by means of a strong faradic current, goose-skin appears for a greater or lesser distance around the electrodes. This goose-skin is not the result of a central reflex but is due to the spread of nerve impulses along a plexus of sympathetic fibres in the skin; the absence of this local reaction of the pilomotor mechanism to faradism shows that the sympathetic nerves have degenerated.

To observe this reaction, Lewis and Marvin employ a du Bois Reymond coil connected to a two-volt accumulator, the current from the secondary coil being carried to twin platinum contacts lying 1½ mm. apart. The secondary coil is placed at such a distance that, when the current is led into the unmoistened skin, it is quite painful; a faradic current of this intensity is usually necessary to get full elevation of the hairs. In about four or five seconds the skin begins to show small discrete elevations, best seen when these are obliquely illuminated; these quickly grow in prominence until full goose-skin is manifested in ten to twenty seconds. Upon the fore-arm the area at first involved extends a centimetre or two from the electrodes in every direction, but if the current is maintained it spreads farther in the skin, until it may involve an area approximately circular and six or more centimetres in diameter; on the leg the area is often larger. It is to be noted that faradic stimulation of the skin also produces the typical reaction to injury, the local red spot, the wheal and the surrounding flare appearing in the skin.

Application of the tests.—The practical application of these two tests is illustrated in the following case of sarcoma of the first rib, complicated by a cervical sympathetic paralysis and later by a paraplegia.

The patient, a girl, aged 18, was admitted to University College Hospital under the care of Mr. W. Trotter in July, 1927. She was pale and thin and had a lump in the left posterior triangle of her neck. This was about eight centimetres in diameter, hard and fixed to the first rib; it was not connected to the spine. The mass extended down into the chest, giving rise to definite physical signs, namely, flattening, impaired percussion note and diminished breath sounds at the left apex; the rest of the chest showed no abnormal physical signs. X-ray examination revealed that the left first rib was much eroded by a neoplasm extending down into the thorax, but the vertebral column was not involved. The Wassermann reaction was negative. An excised portion of the mass was found microscopically to be a round-celled sarcoma. The growth also affected the nervous system at the root of the neck on the left side, the sympathetic nerves being chiefly involved. There was in addition

some wasting and weakness of the left upper extremity, especially of the small muscles of the hand; the distribution was compatible with a lesion involving the sixth, seventh and eighth cervical and the first thoracic anterior roots, or the lower two trunks of the brachial plexus. A lesion of the brachial plexus was indicated by the presence of anæsthesia and analgesia on a narrow strip along the ulnar border of the fore-arm and on the inner half of the palm and the fourth and fifth fingers.

Sympathetic nerves.—Slight enophthalmos was present on the left side and the left palpebral fissure was smaller than the right. The left pupil was greatly contracted; the direct and consensual reactions to light were normal and so was the reaction to accommodation. Although both sides of the face were equal in colour, the left side was a little warmer to the touch than the right. The following representative series of thermo-electric readings were all obtained at a sitting:—

	Right	Left	Difference
Forehead	31·3° C. ..	31·8° C. ..	0·5° C.
Cheek	31·5° C. ..	31·8° C. ..	0·3° C.
Chin	31·7° C. ..	31·9° C. ..	0·2° C.

The left arm was also warmer than the right, the differences in temperature being greater than in the case of the face, although the colour of the two arms was the same. Thermo-electric readings on the skin of the arms were as follows:—

	Right	Left	Difference
Forearm	28·0° C. ..	23·3° C. ..	1·3° C.
Back of hand	25·7° C. ..	28·8° C. ..	3·1° C.
Ring (IV) finger	24·5° C. ..	30·0° C. ..	5·5° C.

The spinal pilomotor reflex was tested by applying a piece of ice to the cervical spine. Goose-skin appeared over the body generally and on the right arm. Goose-skin failed to appear on the left fore-arm and on a part of the left upper arm. The line of demarcation was mapped out; this varied slightly during the process of mapping out, but never by more than half an inch. It may be described as starting on the inner side of the arm 2 inches below the anterior fold of the axilla and running up and out towards the point of the shoulder (A, fig. 1); thence passing down the outer border of the arm to just above the elbow (B, fig. 1), and from here obliquely up the posterior aspect of the arm to rejoin the starting point. All skin proximal to this line was covered with goose-skin (see fig. 1). No goose-skin was detected on the fore-arm. The presence or absence of goose-skin on the face was not noted.

The patient had noticed that for about ten weeks before admission to the hospital her left arm did not perspire, though her right did; she had found, however, that both axillæ perspired freely. On one occasion in the ward, it was observed that her right hand was sweating profusely, whereas the left was absolutely dry. Pilocarpine nitrate ($\frac{1}{4}$ gr.), given hypodermically, produced profuse sweating over the body generally and the right upper extremity, but the left hand and fore-arm remained quite dry. The area of skin without sweat secretion corresponded very closely to the area described above where goose-

skin failed to appear; it was a little less extensive by about half an inch all the way round the arm. The sweat reactions on the face were not noted.

These facts pointed to interference with the sympathetic nerve supply to the left side of the face and left arm. It was not known whether the peripheral fibres for the face were degenerate or not, but the absence of sweating on the fore-arm after the administration of pilocarpine indicated that here the peripheral nerve-fibres were degenerated.

The sympathetic supply to that area was further tested by local faradization on the same day as ice was applied to the spine. Faradic stimulation of the skin of the left arm failed to produce goose-skin over the same area in which

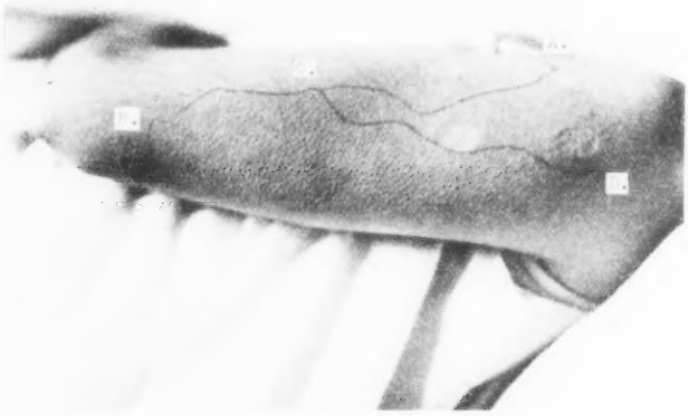

FIG. 1.—Photograph of left upper arm to show the pilomotor response to the application of ice to the cervical spine on November 21, 1927. Distal to the line A—B no goose-skin appeared; goose-skin was more distinct on the posterior aspect of the upper arm behind the line C—D than over the point of the shoulder.

it failed to appear when ice was applied to the spine, and in which sweating was absent after the administration of pilocarpine. Proximal to the line of demarcation already described and everywhere on the right arm good goose-skin developed. On both sides of the face distinct but less extensive goose-skin was obtained. The results of this test confirmed the conclusion that the sympathetic fibres to the arm were degenerated and provided the additional information that the peripheral fibres to the face were intact.

The patient was discharged from the hospital on November 25, 1927, after radium had been applied to the growth in the neck. She was subsequently treated as an out-patient by deep X-ray therapy. Her condition remained unchanged until the end of 1928, when her legs became weak and her gait tottering. She was re-admitted to hospital on November 23, 1928. She was

found to have a paraplegia from the second thoracic segment downwards: this was accompanied by retention of urine with overflow. Severe cystitis subsequently developed and the retention gave place to incontinence. She had not wasted greatly since she was first seen in 1927. Evidence of a secondary deposit in her left lung was found clinically, and this was confirmed by X-ray examination of her chest, which showed a large deposit, about 5 cm. in diameter. In the lower cervical region the primary growth was visible as a large mass invading the first and second dorsal vertebræ, as shown by rarefaction of the

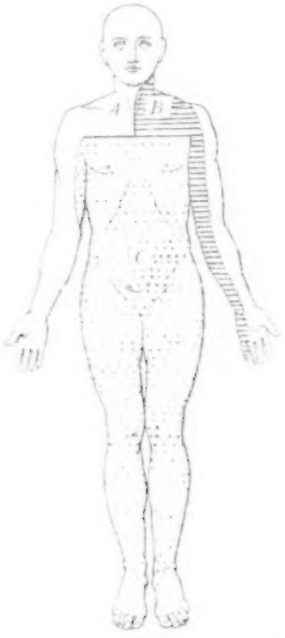

FIG. 2.—Showing area of loss of sensation in December, 1928.

Area A = skin with normal sensation.
Area B = skin anæsthetic as a result of a peripheral nerve lesion.
Area C = skin anæsthetic as a result of a paraplegia.

bodies of these bones. On comparison with the X-rays taken at the end of 1927, it was clear that both these changes were more recent than that date. There was complete loss of movement in both legs; the patient was unable to use her intercostal muscles and employed the diaphragm for respiration. There was no further disturbance of the motor functions of the left arm, as compared with that in 1927. The signs of involvement of the sympathetic nerve supply to left arm and left side of face also remained unchanged; after administra-

tion of pilocarpine it was noted that sweating occurred on both sides of the face.

Sensory nerves.—Sensation was lost over the areas shown in fig. 2. The skin of the body (area *C*) was anæsthetic from the second rib downwards on both sides; the anæsthesia extended also to the inner aspect of the right upper arm. On the left upper extremity the loss of sensation (area *B*) extended down the inner half of the whole limb and up on to the shoulder and trunk. The skin of the face, right shoulder and the rest of the right upper limb had normal sensation (area *A*). The sensory loss over area *C* corresponded to that produced by a destructive lesion of the spinal cord at the level of the second dorsal segment, and here the peripheral fibres were presumably intact. Over area *B* the loss on the arm was most probably due to a lesion of the brachial plexus and the peripheral nerves were presumably degenerated.

Further information as to the state of the peripheral nerves was obtained by applying the flare test. Over area *C* a flare developed after scratching the skin; this showed that the peripheral nerves were intact. Over area *B* no flare appeared, confirming the view that the peripheral nerves had here degenerated. Finally, on normal skin (area *A*) the flare and the usual response to injury occurred. These findings are summarized in the table:—

REACTIONS OF THE SKIN TO INJURY.

Site.	*Sensation.*	*Lesion.*	*Flare.*
Area *A* ..	Normal ..	None ..	Present
Area *B* ..	None ..	Nerve ..	Lost
Area *C* ..	None ..	Cord ..	Present

The patient's condition remaining unchanged, she was discharged from hospital on July 2, 1929. She died at home on August 5, 1929, no autopsy being obtained.

SUMMARY.

Two simple skin tests are described, by means of which it can be determined easily whether the peripheral sensory and sympathetic nerve-fibres are degenerate or not. Their application is illustrated in a case of sarcoma of the first rib, complicated by a cervical sympathetic paralysis and later by a paraplegia.

I am indebted to Mr. Wilfred Trotter for leave to investigate this case, and to Sir Thomas Lewis for much valuable advice and help throughout.

REFERENCES.

[1] LEWIS, T. "The Blood-Vessels of the Human Skin and Their Responses," London, 1927.
[2] LEWIS and GRANT. *Heart*, 1924, **11**, 209.
[3] LEWIS, HARRIS and GRANT. *Ibid.*, 1927, **14**, 1.
[4] LEWIS and MARVIN. *Journ. of Physiol.*, 1927, **64**, 87.
[5] MÜLLER, L. R. *Deutsch. Zeitschr. f. Nervenheilk.*, 1913, **47-48**, 413.

THE RESPIRATORY RHYTHM IN ITS RELATION TO THE MECHANISM OF THOUGHT.

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THE methods hitherto employed in the investigation of the respiratory concomitants of mental activity have been of two types. The total ventilation has been recorded by means of a plethysmograph into which the subject breathes through a mask or mouthpiece, the expired air alone being measured. Another method involves the use of some form of volume recorder strapped round the chest, the respiratory movements being transmitted to a recording tambour.

No one who has experience of the extraordinary sensitiveness of the respiratory mechanism to affective states can doubt that the first method is so liable to subjective variations as to be unsuitable for psychological work. By means of control tests we were able to demonstrate that even with carefully trained subjects any attempt to breathe through an open mouthpiece or mask, that is to say a piece of apparatus which centres the subject's attention on his breathing, invariably gives rise to an abnormal type of respiration, generally associated with hyperpnœa. We feel convinced that for the recording of strictly normal respiration it is essential not only that the apparatus should in no way interfere with perfectly unconscious and unrestricted breathing, but that in addition the subject should, if possible, be unaware of the fact that his respiration is being tested. The use of a plethysmograph of the nature described, with the unavoidable resistance of its inspiratory and expiratory valves as well as that of the tambour itself, is incompatible with such measurements, even apart from the important psychological factor. As corroborative evidence on this point we will only mention the researches of Schall [6] who showed that even a valve with a resistance exceeding 25 mm. of water has a perceptible effect on the respiratory curve.

Turning to the various methods of recording the respiratory movements of the chest and abdomen, it may fairly be urged that none of

these can by its very nature give anything approaching a true record. They are all concerned with recording the movements at a restricted level, i.e., that of application, and can give no definite information as to the resultant effect of the dual mechanism on the total ventilation.

With these considerations in view, we adopted the principle of the apparatus first used by Haldane [4] in his experiments on the excitability of the respiratory centre. In Haldane's original method the subject lay in an oblong box with the head outside, the neck passing through a hole in the lid, composed of an upper and a lower segment. An air-tight junction round the neck was obtained by packing with plasticine. By a suitable volume recorder the increase and decrease of air volume in the box, corresponding to expansion and deflation of the chest and abdomen respectively, could be registered. This simple device is quite satisfactory for the investigation of the physiological responses of the respiratory centre, but requires certain modifications to make it suitable for psychological purposes. We therefore constructed a form of apparatus which allows the subject to be comfortably seated and involves a minimum of pressure round the neck. Our first attempt was not quite successful in so far as the recording instrument proved too insensitive to respond to small and rapid respiratory movements, also in that we had considerable difficulty in obtaining a perfectly air-tight joint round the neck. Professor Buckmaster and Mr. Hickman had meanwhile overcome both these difficulties in an apparatus of similar construction which they used for some unpublished work on respiration in the Physiological Laboratory at Bristol. We are indebted to them for the advice that led to the reconstruction of our plethysmograph on lines substantially similar to the apparatus at Bristol. Fig. 1 shows the final form of the apparatus as used in the present experiments. Essentially it consists of a wooden box with a removable lid and front-piece, both of which can be clamped firmly into position by means of large handscrews. All the joints on the box are effected by the interlocking of carefully moulded edges, the corners being in addition padded with strips of felt. The joints have remained wholly air-tight after more than a year's usage. The lid consists of two pieces, the back being fixed to the box, the front being detachable; both have semicircular holes in the centre, which together form the opening for the neck. The lid is inclined at an angle of 73° to the back of the box, this having proved a detail of great importance, since the neck emerges from the lid not vertically but at an angle. A horizontal section of the neck gives an oblong outline, and considerable discomfort to the subject would

therefore result should the neck-hole be in the wrong plane while remaining strictly circular. A circle had to be adopted on account of the great difficulty of achieving an air-tight joint with an elliptical aperture. The diameter of the neck-hole is sufficient to allow of about $\frac{1}{2}$ cm. free play with large-sized necks. An air-tight joint round the neck is obtained in the following way: an inflatable rubber collar with an 8-in. circular skirt attached is slipped over the head and inflated so as to fit the neck exactly, without causing pressure and discomfort. The subject having been seated in the box and the front half of the lid clamped on, the skirt is spread evenly over it. A pair of boards con-

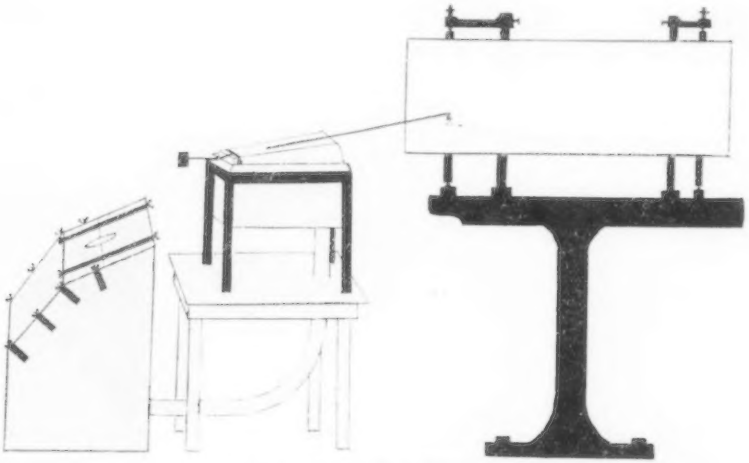

FIG. 1.—Sketch of apparatus.

sisting of right and left segments, cut so as to cover the lid exactly, are then placed on top and securely bolted down on the lid. The clamping down of the front piece completes the preliminaries. It is a matter of some importance in ensuring the comfort of the subject to test the height of the seat and alter it, if necessary, before fixing the lid in position. Too low a seat, helped by slight sinking into the cushions, is liable to cause the subject to be partially suspended by the chin and so give rise to discomfort and restlessness: while too high a seat brings the shoulders up against the lid and causes undue fatigue of the neck muscles in holding the wholly unsupported head upright. We obviated this latter difficulty by slipping on a second and loosely fitting collar which, when inflated, acts as an air-cushion for the head, allowing of

complete muscular relaxation. A second important point is to pad the box so that the subject has a rest for his back, as otherwise the head tends to bend forward and fall lower and lower. We have had subjects supported in this manner who slept in the box for over two hours without afterwards being aware of stiffness in the neck or any other untoward effects.

The air space in the box communicates with the recording plethysmograph by a wide tube carefully bent so as to avoid acute angles, thus minimizing the resistance to the air current. For this purpose also the tube should be at least 6 cm. in diameter; a smaller bore occasions lag and inadequate sensitiveness of the recorder.

The recorder itself is of the familiar float pattern, rectangular and having a capacity of about 4 litres. The float is balanced on knife edges at its posterior end, the edges resting in corresponding notches on the wall of the trough. A screw projection from the back of the float holds an adjustable weight by means of which the angle of the float and hence the level of the writing point can be altered. A light rod, acting as stylus, is fixed to the top of the float and projects 45 cm. in front. At the end of it is a small writing point fed with red ink which writes on white glazed paper. The up-and-down movement of the lever describes the arc of a circle (with the lever as radius), so that the pointer must be able to swing backwards and forwards on a hinge in order to remain in contact with the vertically placed paper. The front wall of the float is curved, so as to form an arc similar to that represented by the excursion of the lever. The damping effect of the water bath renders the excursions dead beat, while the absence of resistance to the air current allows exceedingly small and rapid movements to be registered.

By means of a small side opening in the box the whole system can be brought into equilibrium with the outside atmosphere before finally making it air-tight and beginning the experiment. The sensitiveness of the apparatus is such that it can be made to show individual heartbeats quite plainly on the respiratory curve.

The excursions of the pointer are calibrated in terms of volume per millimetre excursion, so that an accurate determination of the total ventilation can readily be made when required.

Control tests have shown that slight movements on the part of the subject in the box have no effect on the respiratory record so long as the apparatus remains perfectly air-tight. We always make a point, however, of asking our subjects to keep particularly quiet once they

have found a comfortable position, nor did it happen more than once or twice that records had to be discarded on account of movement when reasonable precautions were taken to make the subject as comfortable as possible.

Throughout our experiments we have abstained so far as possible from any suggestion to our subjects that we were investigating the rhythm and volume of respiration. Although the majority of them were either medical students or qualified medical men and women, we found that most of them unhesitatingly accepted the suggestion conveyed in very vague terms that the object of the experiment was a metabolic investigation, and paid no attention to their breathing. We attached great importance to this point at first, since there is no question but that the psychological factor is of great importance in such experiments. However, subsequent observations on ourselves and subjects who had already been experimented on, and therefore knew the purport of the apparatus, have tended to show that under the conditions of the experiment there is little to be feared from the knowledge that respiration is being investigated. By allowing a few minutes to elapse (ten on an average) from the time at which the subject is first seated in the box to the commencement of the actual experiment, it was easy to satisfy ourselves, both by questioning the subjects and examination of the records, that breathing was always normally and unconsciously performed.

Subjects.

The subjects examined were forty-five women and twenty-five men. Of the women thirty were medical students or newly qualified practitioners from the Royal Free Hospital. Of the remainder, five were occupied in scientific work and ten in literary and artistic work. Of the men twenty-two were either medical men attached to the mental hospitals service or trained scientific assistants in the laboratory, one was a young mathematician, one a barrister and one a business man. The great majority of our subjects were therefore trained in a scientific occupation and with ten exceptions they were under 35 years of age.

In the present series of experiments we found that when the subject sat in an unoccupied state in the box we were at once able to demonstrate the existence of two types of respiration. In the one type the rhythm and the amplitude of the respirations remained absolutely regular ; in the other both the rhythm and amplitude were exceedingly irregular. Pauses of varying length occurred between the respirations and the total ventilation might vary several hundred per cent. between

any two successive breaths. It was further noted that even in the cases of disturbed respiration the subject tended to maintain the total ventilation over any considerable period at the same level by compensating for a small breath by one or more succeeding large ones, or by following a lengthy pause by respirations of either increased frequency or increased size. This compensation alone, apart from numerous control experiments, demonstrated that the irregularities could not have been caused by movements other than those of respiration, e.g., fidgeting in the box.

FIG. 2 A.—Respiratory record of a "visual" subject during rest and mental arithmetic. The subject is engaged in adding up columns of figures between the two crosses. Lower line time in minutes. Note the uninterrupted regularity of the breathing at onset and cessation of work. Reduced to ½.

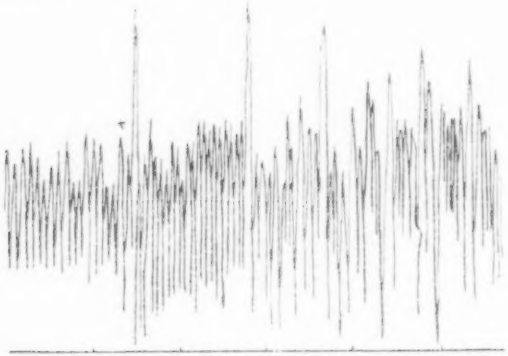

FIG. 2 B.—A record taken under exactly similar circumstances as A and belonging to an "auditory" subject (B). Onset of calculation at the cross mark. Lower line time in minutes. Reduced to ½.

It was noted that the type of breathing, regular or irregular, remained constant on repeated examination of any one subject and that it maintained its character even after the subject had been in the box for over an hour. It did not appear likely that such peculiarities in the apparently resting subject could be ascribed to fluctuations of attention.

The next step was to see how subjects of the two types reacted to a task requiring some concentration of attention. For this purpose a page of figures arranged in ten columns (thirty-six in each) for simple addition was placed before the subject. It was found that subjects who

had previously exhibited a regular rhythm persisted in this during the performance of the task. In those subjects who showed irregular breathing during the resting stage the performance of the arithmetical task was accompanied by the same or sometimes a higher degree of irregularity in rate and amplitude. The time occupied by the addition averaged seven minutes, and throughout this period the two types of respiratory rhythm maintained their characteristics. The subjects were

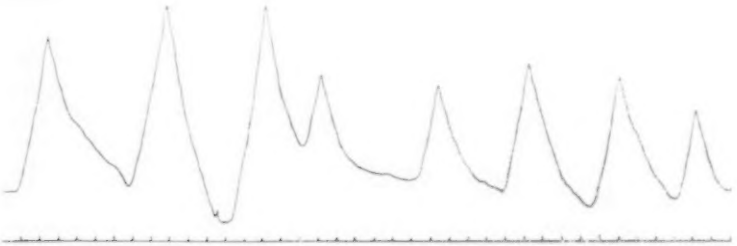

FIG. 3.—Record of subject B at rest, taken at a greater speed. Lower line time in seconds. Reduced to ⅓.

not enjoined to make any very intense effort: they were asked to aim at accuracy but not to communicate their results. Occasionally during the first few seconds of calculation a more or less complete inhibition of respiration made its appearance. We are not here concerned with this transitory phase, which rarely lasts longer than half a minute and corresponds to the initial increase of tonus with mental effort, and which will be discussed later.

FIG. 4.—Similar record of subject A taken at exactly the same speed. The contrast between the two types is well marked. The differences in size of excursions are due to the fact that subject B is a tall man and subject A a woman of rather less than average height. Reduced to ⅓.

Fig. 2 shows two very typical records, A being that of a subject exhibiting a markedly regular rhythm, and B of a subject showing great irregularity. It will be observed that addition causes no change in the rhythm of A, whilst in B the irregularity becomes more pronounced. Fig. 3 is a record of irregular respiration of subject B at rest taken at a greater speed. It reveals the complete irregularity of both rhythm and amplitude, with the tendency for succeeding groups of respirations

to compensate for variations of their precursors, so as to maintain the total ventilation per unit time at the same level. Careful measurements of the excursions of the lever reveal a complete uniformity of the total ventilation over long periods both in the resting and working subject. Fig. 4, which represents the respirations of subject A during rest, is taken at exactly the same speed as fig. 3, and shows the difference between the two types very strikingly. In the regularly breathing subject the effect of intellectual work is sometimes to cause a uniform lengthening of the expiratory phase, which may be accompanied by an increase in total ventilation without, however, causing an irregularity of the rhythm.

If the two classes of subjects be now asked to recall firstly a piece of poetry and next a piece of music, the reaction is in the main the same as that obtained during calculation: the regular rhythm of the one remains unaltered, and the irregularity of the other is increased. The same result is obtained when the two types are asked to assemble silently the arguments *pro et contra* of an abstract problem, e.g., the freedom of the will.

A concrete problem of the following nature is now set: The subject is asked to imagine that he is given a number of 1-inch cubes which he is to arrange in such a way as to form a large cube measuring 3 in. a side. The large cube is then to be painted red all over and taken to pieces. The problem consists in working out how many of the little cubes will have three sides, two sides, one side painted red, and how many will have no paint at all. The effect of this puzzle on the respiratory rhythm is different from that of an abstract problem. Whilst the subjects with a regular rhythm continue to breathe regularly during the silent unravelling of the problem, the majority, i.e., 80 per cent. of a group of twenty-five irregular breathers, become regular with the onset of this task. Fig. 5 shows the effect of this problem on the respirations of subject B. Of the five who continued to breathe irregularly, two, on being questioned, averred their inability to deal with the problem, which they therefore abandoned, but there is unfortunately no record of the remaining three being questioned on this point.

So far, then, we have distinguished two types of respiratory behaviour, both of which persist whether the subjects be engaged in arithmetical work, in recalling poetry, or music, or in solving an abstract problem, but which alters when a problem involving purely visual imagery is attempted—the regular type persisting, and the irregular type becoming regular.

A total of sixty-seven subjects were examined on these lines, and 45·5 per cent. gave records characterized by an irregular respiratory rhythm, whilst 54·5 per cent. showed a regular rhythm.

The persistence of the two types of respiration under varying circumstances made it appear extremely improbable that the irregularity of the one type was due to fluctuations of attention, while the fact that an irregular rhythm became regular when an attempt was made to solve a problem requiring visual imagery pointed to a relation between the respiratory rhythm and some factors in the mechanism of thought. We therefore proceeded to obtain introspective evidence from each subject as to whether he or she was conscious of relying chiefly on visual or verbal imagery in thought. In this inquiry we were confronted

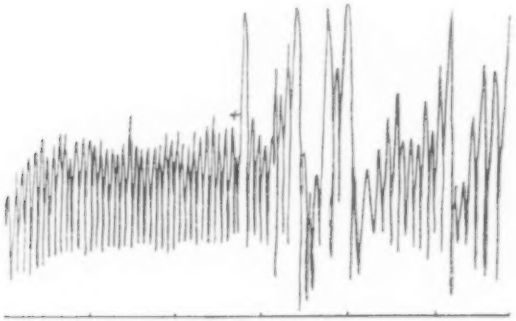

FIG. 5.—Record of subject B while engaged in solving a problem requiring visualization and during subsequent rest. Work to the left of the cross mark, rest to the right. Lower line, time in minutes. Reduced to ½.

with some difficulties which are less apparent in investigations undertaken on subjects trained in a psychological laboratory. Very few of our subjects had any psychological training or were specially interested in psychological problems; some of them were technicians with only a relatively small amount of the type of education that would be helpful in an introspective inquiry into mental mechanisms. All our subjects were busily employed, many of them in working for examinations, and had at considerable self-sacrifice found the time to attend at the laboratory for the experiments. To have subjected them all to an elaborate questionnaire demanding considerable psychological acumen on the part of the respondent would have been to obtain a small selection of utilizable answers which, for all we knew, might have been representative of only one type of thought mechanism. We therefore decided

to submit a few relatively simple questions which would admit of some form of answer from anyone of average intelligence, and to assess the predominant type of thought mechanism on the answers given. These assessments were made without any reference to the plethysmographic records, the correlation of the two being left to the end. The questions which were submitted, either in writing or orally, and on which our assessment was based, were as follows:—

(1) To what extent do you think (*a*) in terms of your own voice, (*b*) in visual images, and (*c*) in terms of movement? Do any of these processes occur simultaneously? If (*a*), are you aware of any throat or tongue movements when thinking?

(2) When you recall a piece of prose or poetry do you hear it or see it? Is it accompanied by visual or auditory images of the events in the piece apart from the actual words?

(3) When you think of a person or object do you first have to recall individual features in order to reconstruct the whole, or do you see them as a whole? If you have to recall individual features do you have to name each before you see it?

(4) In recalling a piece of music do you do so in terms of your own voice or of an instrument?

(5) When calculating how do you represent the figures to yourself?

A number of other questions dealt with points which will be considered later, but it was on the answers to the above five that our subjects were assessed as either predominantly making use of visual or of auditory imagery in thinking. On comparing this classification with the type of record obtained with the plethysmograph, we found that subjects assessed as predominantly visual gave a record of quiet regular breathing, and that those belonging to the auditory type exhibited an irregular respiratory rhythm.

Of the sixty-seven subjects examined introspectively and plethysmographically the records of thirty-four showed a regular respiratory rhythm under all circumstances. Of these, thirty-three were assessed by their own account of themselves as being predominantly visual and one only as belonging to the auditory type. The records of thirty-two subjects showed an irregular respiratory rhythm and of these twenty-eight were assessed by their answers as being of a predominantly auditory type, whilst four were judged to be visual. One record was rejected owing to continuous movement on the part of the subject while in the box, masking the true respiratory picture.

Thus of the sixty-one cases in which records and questionnaire agreed,

54 per cent. belonged to the visual type with regular breathing and 46 per cent. belonged to the auditory type with irregular breathing. Considering the fact that our questions were admittedly lacking in psychological precision, it is surprising that the discrepancies only totalled 7·5 per cent.

The distribution of the two types is about the same in the two sexes. Our sixty-one subjects comprised twenty-one men who were divided into ten of the auditory and eleven visual type, whilst of the forty women twenty-three belonged to the visual and seventeen to the auditory type. Since the overwhelming majority of our subjects were either connected with medicine or science no occupational classification is possible.

The Significance of the Two Types of Respiratory Rhythm.

The fact that irregular breathing becomes regular when a problem such as that of the cubes is set—a problem that can only be solved by visual imagery—is in itself a strong indication that the irregular respiration recorded in the auditory type is causally connected with the predominant use of internal speech, at the existence of which our subjects hint when they say that they think in terms of their own voice. The image here is an auditory one but invariably refers to the subject's own vocal organs. It would, however, be wrong to assume that such irregularity both of rhythm and amplitude of respiration is in any sense a point-to-point representation of the actual respiratory disturbance that would take place were the auditory images to be translated into spoken words. If this were so, such images could only occur, as in speech, during the expiratory phase, whereas anyone belonging to the auditory type is conscious that the images arise uninterruptedly both during expiration and inspiration. Such a person has only to maintain an imaginary argument in terms of internal speech to satisfy himself that the stream of auditory images undergoes no interruption during inspiration. The irregular breathing of an auditory person cannot therefore be regarded as a mere silent reproduction of the respiratory movements that would take place were the words audibly spoken or whispered. That states of emotional and intellectual tension are accompanied by respiratory disturbances has long been known. It is necessary to discuss shortly the possibility of mental tension as a factor influencing respiration.

Our primary object in this investigation had been to see whether any correlation could be found between lapses of attention and disturbances

in the respiratory rhythm. The effect of intensive intellectual effort on respiration, such as shallow and quickened breathing, and the occasional occurrence of inhibition in the inspiratory phase, has been repeatedly studied by observers using thoracic and abdominal recorders of the Lehmann type. Zoneff and Meumann [7] from numerous observations on six subjects were able to state that voluntary concentration of attention causes a slowing of the pulse and an inhibition of respiration more marked in the thoracic than in the abdominal type; also that the inhibition appears either in the form of a total cessation, or in a flattening of respiration which is often accompanied by an increased frequency; that the inhibition of respiration and slowing of pulse rate reach a certain maximum intensity, and then, if the experiment be continued, they again become normal or even swing over to the opposite side. They conclude that the alterations of the respiratory rhythm are linked up with fluctuations of attention. One of us [2] in 1921 described similar phenomena and endeavoured to show that they bore a relation to the increased tonus of skeletal muscles which it was possible to demonstrate by myographic methods during intellectual effort and which we have recently confirmed by observations on the tendon reflexes [3]. In all such cases the experiments have been of short duration and the attention has been concentrated with maximum intensity.

Apart from the fact that our experiments were conducted over lengthy periods under conditions which involved no great increase of emotional or intellectual tension, two facts emerge that negative the explanation that respiratory irregularity is due to either or both of these factors. Firstly, the correlation between the auditory type and irregular breathing, and the visual and regular breathing, which would on this hypothesis imply the manifestly absurd assumption that only the auditory type display intellectual and emotional tension. Secondly, that when the auditory type concentrates on a problem that can only be tackled by the use of visual images the respiration becomes regular, except in those subjects who declared that they were unable to conjure up the necessary image and abandoned the attempt to solve the problem.

Can the respiratory irregularity be explained as being due to interference of laryngeal movements accompanying auditory images? One of us has been able to produce objective evidence that such laryngeal movements may occur during the representation of singing up and down an octave, but there is no such objective evidence of their general occurrence during thought processes of the auditory type. Stricker, by introspection and concentration of attention upon his own mental

processes, came to the conclusion that the primary revival of word images was by a sense of movement in the muscles of articulation, but, as Mott [5] points out, any such concentration must make the observation of doubtful value. Of our own subjects, ten only were conscious of laryngeal movements during thought, and one described tongue movements. All these subjects, it is to be noted, belong to the auditory or irregularly breathing type, but they form a very small proportion of the total number. It would be unwise, however, to conclude from the fact that the majority of auditives are unconscious of such movements, that they do not occur. As anyone may prove for himself, it is a matter of great difficulty, even when speaking aloud, to apprehend laryngeal movements.

In the absence of any experimental evidence the nature of the connection between irregular breathing and an "auditory" way of thinking must be left an open question. It is at least a possible hypothesis that the continual occurrence of laryngeal movements as an accompaniment or possibly a precursor of verbal images disturbs the respiratory rhythm so as to produce either acceleration or retardation and increased or decreased amplitude of breaths, according to the phase of respiration in which such movements occur.

The Relation of the Two Respiratory Types to Certain Mental Processes.

By far the simplest mental process with which we are concerned is an ordinary arithmetical operation; addition or subtraction, multiplication or division involve a minimum of valuation. To a great extent simple arithmetical operations are memory processes in which the terms of reference are a highly restricted series of images whose nature will be determined by the type originally employed in the process of learning, be the image a visual, auditory or motor one. An inquiry was made among our two classes of subjects as to their proficiency in mental arithmetic. We were, of course, precluded by the status of our subjects from obtaining information by any direct examination such as might be made with junior students. The subject was simply asked: Are you good at mental arithmetic? Of the fifty who answered this question twenty-two reported themselves as bad and twenty-eight as fair or good. Of the twenty-two "bad" cases fourteen belonged to the auditory (irregular) and eight to the visual (regular) type. Of the twenty-eight "good or fair" ten belonged to the irregular, and eighteen to the regular respiratory type.

It may, therefore, be fairly stated that irregular respiration indicates a type of mind that is on the whole unsuccessful in mental arithmetic, and that the opposite is true of the regular breathers. The connection that we have demonstrated between the type of respiration and the type of image predominant in thinking might at first suggest that the failure of irregular breathers to make good at mental arithmetic was due to their being unable to form visual images of the necessary figures. Such an explanation would, however, be an over-simplification of the problem. When asked how they represented numerals, of fifty subjects who replied to this question eleven reported auditory images alone, and of these six belonged to the irregular and five to the regular breathers. Eight reported mixed auditory and visual images and of these six were of the irregular and two of the regular type. The remaining thirty-one subjects all reported purely visual images and of these nineteen belonged to the regular and twelve to the irregular respiratory type.

The data may be summarized in the following table.

Representation of numbers in terms of	Regular breathers		Irregular breathers		Total
	Mental arithmetic		Mental arithmetic		
	Good	Bad	Good	Bad	
Auditory images	2	3	1	5	11
Visual and auditory images	2	—	4	2	8
Visual only	14	5	5	7	31
Total	18 69·2 %	8 30·8 %	10 41·6 %	14 58·4 %	50

It will be seen that though out of our original sixty-one subjects twenty-eight with irregular respiration had reported themselves as predominantly using auditory images in ordinary thought and thirty-three of the regular type as predominantly visual, the imagery of numbers does not closely follow that of thought generally. It will at the same time be noted, however, that when—owing possibly to methods of education—twelve of the irregular auditory type adopt visual number images they are still less successful in mental arithmetic than the regular type using their predominant visual imagery. A possible explanation is that the first-mentioned type of person visualizes numbers very imperfectly and carries on his mental arithmetic by interpolating verbal processes with the visualized numbers. The fact that his respiration continues to be irregular is in favour of this hypothesis. On the other hand, those few cases of the regular type who have adopted auditory

number images do not seem to be as successful in mental arithmetic as the remaining majority of them who retain their visual imagery during calculation. The researches of Galton [1] show how very much further the examination of the visual representation of numbers should be pushed in order to account for divergencies in arithmetical ability between different persons who equally lay claim to visual imagery. The use of what Galton terms "number forms," i.e., the arranging of numbers in various patterns in one's field of vision, which memory faithfully reproduces every time an arithmetical operation is undertaken, is probably nearly as important as the question of what type of number imagery is relied upon. It seems at least a plausible supposition that the mathematical faculty is intimately connected with visualizing powers. A person who need merely refer to a systematically-arranged pattern of figures when called upon to work out an arithmetical problem is manifestly better off than one who has to rely on the slower and more elaborate method of summoning the figures by name, as it were, before they can conveniently be used for reference. Even then it is probably but a transitory image that is evoked, whereas any process beyond the simplest addition or subtraction would require the simultaneous representation of a number of figures persisting over varying intervals of time.

We were not satisfied that under the conditions of our experiments it was possible to obtain statistics of value as to ability in higher mathematics or literature. Answers to our questionnaire on these points might give the impression that ability in both was evenly divided between our two types of subjects, but certain cases in which we had other means of judging tended to show that autobiographical information of this sort is very unreliable. The same remarks apply to proficiency in drawing unsupported by objective corroboration. It was decided for this reason not to push our investigation into specific abilities with reference to the two respiratory types any further.

It seemed, on the other hand, that since we knew a large number of our subjects particularly well, either as pupils, colleagues, or fellow-students, it might be of value to correlate an assessment of their general ability with their respiratory type. Here, again, we could not, with our class of subjects, contemplate any form of investigation on the lines of Spearman. We decided to consider our subjects simply in the unscientific light of general impressions. Those whom we considered as possessing intellectual ability that distinguished them from the mediocre we classed as being of superior intelligence, the remainder as being of

average intelligence. It must be our apology for introducing such unscientific methods into a psychological investigation that the experience of daily life shows that such impressionistic assessments do in practice prove of value when a fair degree of intelligence and common sense can be claimed for the assessor. Fifty-four subjects, thirty of the regular (visual) and twenty-four of the irregular (auditory) type, were assessed on the lines indicated, the assessor in forming his judgment being of course ignorant of the type to which any given subject belonged.

It was found that of the thirty of the regular respiratory type, nineteen, or 63 per cent., had more than average intellectual ability; of the twenty-four irregulars eighteen, or 80 per cent., were of more than average intelligence. The type of subjects on whom our investigations were made should obviously furnish a fairly high percentage of persons of superior intelligence. The subject is to be pursued in further investigations conducted by Spearman's methods on a number of scholars.

The Musical Faculty.

The presence or absence of the power of correctly appreciating musical tone (the musical ear) admits of a fairly clear-cut answer that should provide definite statistics with even such a superficial form of inquiry as our questionnaire. We had small hopes of finding any difference in the distribution of the musical ear between the two types of breathers, as we were disposed to believe that the presence or absence of this faculty depended upon the anatomical features of the cochlea. The appended results have, however, led us to change our views.

Fifty-two subjects were examined, of whom twenty-four belonged to the irregular type (auditory) and twenty-eight to the visual. Of the former, 46 per cent. reported "no ear"; of the latter, 18 per cent. reported "no ear." The subjects were next asked how they would recall a piece of music—whether in terms of their own voice or in terms of the instruments on which they had heard it played. The results can be tabulated as follows:—

Music recalled in terms of	Regular breathers		Irregular breathers		Total
	Musical ear		Musical ear		
	Good	Bad	Good	Bad	
Own voice	3	4	4	9	20
Instruments	20	1	9	2	32
Total	23 82·1 %	5 17·9 %	13 54·1 %	11 45·9 %	52

It would appear, then, that the irregular respiratory type with the predominantly auditive imagery tend in a little more than half the cases to use the same kind of auditory imagery (i.e., thinking in terms of their own voice) for the representation of music, and that this mode of reproduction may in the majority of cases be responsible for a bad musical ear. If this be so, it should be an indication for encouraging children with a "bad ear" to try to represent notes in terms of an instrument rather than by vocal imitation.

Power of Visualizing Faces.

It might be expected that if our correlation between the types of breathing and types of mental imagery were correct a certain difficulty would be experienced by the auditory type in visualizing the features of absent friends. In answer to our questions, ten subjects of the irregular type reported that when thinking of a person they have first to recall individual features in order to reconstruct the whole, and fourteen that they see the face as a whole. Of twenty-seven visual ("regular") subjects, all claimed to see the face as a whole. Of the ten first-mentioned, every one finds it necessary to evoke the dominant features from which the face is reconstructed by a verbal image. Ten of the fourteen who see the face as a whole are also aware of using some form of auditory image in the process. None of the "regular" subjects confesses to the use of any verbal images in reconstructing a face.

Dream Imagery.

Forty-six subjects were able to give some account of the nature of their dream imagery. Twenty-seven have purely visual dreams, and of these twenty-two belong to the regular type of breathers, the remaining five being of the irregular type. Seventeen have mixed auditory and visual images in their dreams, and of these, six are of the regular and eleven of the irregular type.

Two subjects have purely auditory images and both belong to the irregular type.

The Sense of Smell.

Though not strictly in the line of this investigation, we mention the effect on respiration of mental representations of various smells. The majority of subjects who confessed to a keen sense of smell showed very slow and prolonged inspirations interrupted by short and rapid expirations when thinking of a pleasant smell, such as that of a rose. If, after a rest, they are asked to imagine some unpleasant smell, e.g., that of the post-mortem room, the rule is an immediate and long expiration,

even if the respiratory cycle is thereby interrupted at the beginning of inspiration. The expirations continue to be drawn out as long as the representation of the smell lasts, but after a few seconds the subject usually becomes aware of his disturbed breathing and often guesses the purport of the experiment. On account of this we invariably introduced the question of smells at the end of the experiments. In every case where a pleasant smell failed to produce a response the subject afterwards declared that he was quite unable to imagine it.

The Persistence of the Two Types of Imagery.

Although no data are obviously possible as to the persistence of our two respiratory types throughout life, our subjects were unanimous in declaring that so far as they knew no change had occurred in their particular type of imagery since childhood. Galton considered that he had evidence of auditory imagery gradually replacing visual imagery with advancing age. As most of our subjects were under 30 years of age and none over 50, it is impossible to control this statement.

General Observations.

Our inquiry has only been directed to discover a correlation of some type of thought process with the two very distinct respiratory types that have just been described. Up to the present stage we have abstained from a more detailed investigation into the very complex forms of imagery which the researches of Galton and others have demonstrated, and which may throw some further light on our two respiratory types. Of a motor or dynamic imagery, we have found no very definite trace in the superficial inquiry directed to our subjects. We would wish, moreover, to emphasize that we claim to have demonstrated in the case of the irregular type of breathers only the bodily concomitants of certain forms of imagery, forms that constitute not thought in its entirety, but a series of sign-posts which mark the direction of the continuous stream of thought, that is, of the sense of relation of which we have no definite image. Though two streams, marked either by visual or auditory sign-posts, may ultimately arrive at much the same final conclusion in concrete problems, evidence is not wanting to show that psychological and metaphysical speculations will be profoundly influenced by the type of imagery adopted. We would venture, for example, to suggest that the extreme form of behaviourism put forward by its chief exponent is in no small degree influenced by the fact, so apparent in all his writings, that he is an extreme example of

thinking in terms of auditory imagery. The possibility of determining by objective methods the predominant type of thought imagery may prove to be of some practical value in assessing the fitness of subjects for certain specialized forms of work.

Conclusions.

Observations were made on the respiratory volume and rhythm by means of a plethysmograph enclosing the whole body. Two types of habitual respiration have emerged and are approximately equally distributed among normal subjects of both sexes. The irregular respiratory type has been found in subjects with predominantly auditory imagery; the regular type in subjects with predominantly visual imagery. The irregular type has been found to become regular when a problem is tackled the solution of which requires purely visual images.

The regular type are superior to the irregular type in mental arithmetic.

The "ear for music" is found to be more developed in the regular type. The irregular type tend to recall instrumental music in terms of their own voices.

The power of visualizing faces is much better in the regular type.

General ability was found to be higher in the irregular type.

Purely visual dreams are more frequent in the regular type; mixed visual and auditory dream imagery in the irregular type.

In conclusion, we have to thank Professor Buckmaster and Mr. Hickman for advice in improving our apparatus, and our many subjects for their kindness in subjecting themselves to lengthy experiments and to the questionnaire. Our special thanks are also due to the Medical Research Council for a grant which has enabled one of us to undertake collaboration in this piece of research.

Bibliography.

[1] Galton. "Inquiries into Human Faculty," 1883.
[2] Golla, F. Croonian Lectures, *Lancet*, 1921 (II).
[3] Golla, F., and Antonovitch, S. *Journ. Mental Science*, 1929, **75** (No 309), 234.
[4] Haldane, J. S. "The Regulation of the Lung Ventilation," *Journ. Phys.*, 1905, **32**, 242.
[5] Mott, F. "The Brain and Voice in Speech and Song," London, 1910.
[6] Schall, L. *Zeitschr. f. d. ges. exper. Med.*, 1921, **14**, 322.
[7] Zoneff and Meumann. "Effect of Attention and Mental Work on Respiration," Wundt's "Philosophische Studien," **18**, 1.

ELECTROMYOGRAPHIC STUDIES OF VOLUNTARY MOVEMENTS IN PARALYSIS AGITANS.[1]

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Amongst the cardinal clinical features of paralysis agitans the most characteristic and constant are:—

(i) an increased resistance to passive movement,
(ii) involuntary tremor of characteristic form,
(iii) certain disorders of voluntary movement; notably, slowness,
(iv) certain typical attitudes.

A certain degree of lack of parallelism in these features, both in the matter of their relative intensity, and in that of the factors by which they are influenced, suggests that disturbance of more than a single mechanism or function is in question, and that we cannot assume them to be but different manifestations of disorder of a single mechanism. For example, we may not assume that tremor is but an intermittent exhibition of rigidity.

In the examination of the problems thus indicated it seemed probable that simultaneous records of the tension development, length and electrical condition of the muscles might throw some light upon the mechanisms whose activity produces, or whose impairment permits, the development of the disease mentioned above. The graphic records obtained from normal subjects and from those presenting signs of Parkinsonism show, upon comparison, certain differences which indicate the existence of several factors in the production of the Parkinsonian state.

The components of the clinical picture studied by the graphic method are tremor, voluntary movement and rigidity, the three being stated in the order of their accessibility to examination.

The tremor.—The rhythm of the tremor is sufficiently slow to permit its study by simple inspection, but graphic recording is essential for purposes of comparison with the electrical responses obtained from the tremulous muscles. Such electrical records show that there occur

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within the muscle rhythmical outbursts of activity which are synchronous with the mechanical activity which expresses itself as tremor.

The voluntary movements.—While simple observation shows these to be abnormally slow in initiation and execution, graphic recording reveals further that they are abnormally steplike or discontinuous in performance. Further, the voluntary movements of normal subjects similarly recorded under comparable circumstances also present a step-like discontinuity of performance not in quality different from that seen in paralysis agitans. A comparable feature in voluntary movement was first described by Schafer in normal subjects [3], and a comparative study of the phenomenon in normal subjects and in those suffering from paralysis agitans led Walshe to suggest that in the latter we see the exaggeration of a discontinuity that is present in the voluntary movements of normal subjects [4].

Electrical records show certain prominent features which are clearly related to those found in myographic records.

The rigidity.—Myographic records of passive flexion and extension of the fore-arm have been made. In making these it is clearly of importance that records so made should be in terms of angular rotation about the elbow-joint: i.e., the force should be a constant couple and not a linear pull, while the record should show equal deflections for equal degrees of rotation of the fore-arm upon the upper-arm.

By the recording of passive movements in this way we are enabled not only to measure various arbitrary degrees of shortening of the muscles concerned, but also to examine the distribution of the resistance to such movement resulting from the rigidity of the muscles. Since the external force is a constant couple, any variations from a theoretically constant angular acceleration must be due (apart from inertia) to variations in the resistance of the muscles stretched, and is proportional at any stage of rotation to the resistance in play at that moment. The recording of rotation at the elbow, and not merely of some linear trajectory of a point on the limb, provides a record in terms of that mechanical function for which in practice the muscles are normally activated.

Records obtained from electrical leads inserted into a muscle subjected to stretching as in the above experiments are of too uncertain value to be usefully assessed, because the gross changes in the length of the muscle entail so much shifting of the electrodes in relation to the muscle tissue that a complex electrical disturbance is produced, in which the actual muscle action-currents are with difficulty recognized.

Description of the Apparatus.

The method adopted for the recording of electrical changes within the muscle during activity was that first described by Adrian and Bronk [1]. A hypodermic needle carrying in its lumen an insulated electrode is pushed through the skin into the underlying muscle. Leads are taken from the needle and from the electrode passing through it and connected to the input terminals of an amplifying apparatus. The amplified output from this is connected both to a loud-speaker and to a a Matthews' oscillograph. When the muscle is active, a change of potential occurring in the immediate neighbourhood of the electrode gives after amplification, an induced current in the loud-speaker which produces a "crack" or a "pop," and a deflection of the oscillograph mirror which may be recorded photographically.

The standard practice has been to get the subject of the experiment either to contract his muscle as steadily as possible against a certain constant force, or else to vary the tension in his muscle gradually and progressively between certain limits. The deflections of the oscillograph are photographed while this is being done.

Some of the components of this apparatus were of standard type, some were convenient modifications of previously described units, and others were devised especially for this particular work. Each in turn will be shortly described.

The external insulation.—The patient and the apparatus in direct connection with him is entirely enclosed within a rectangular cage made of perforated zinc supported upon a light wooden framework. This is 8 ft. long, 6 ft. high and 3 ft. wide, and can accommodate either a table and a chair, a couch, or a standard bench for animal experiments. It is connected to earth independently through an unearthed pipe.

A second cage of the same material completely encloses the amplifying apparatus together with all the batteries and leads which are used in connection with this. It, also, is earthed independently in the same way.

The loud-speaker is contained in a wooden box which is lined with zinc, and the lining is earthed by connecting it to the insulating cage around the amplifying unit.

The connections between these three insulating-surrounds, and with the oscillograph, consist of lead-covered cables, the covering being in every case earthed.

The muscle "Tensometer." (Fig. 1).—The subject sits upon a chair

close up to a heavy table so placed that he can rest his chest against the edge of this and rest both arms completely supported with the fore-arms and upper-arms lying upon its surface.

Upon the top of this table, which is covered with linoleum, is placed the apparatus against which the subject makes those voluntary tension efforts which lead to contraction of his triceps muscle. It can be bolted through the table top in two positions to allow of its use with either arm. It consists of a flat plate of $\frac{3}{16}$ in. brass on which is bolted a small hand vice so placed that its jaws are vertical. Within those jaws can be clamped any one of a series of laminar springs. This spring then ex-

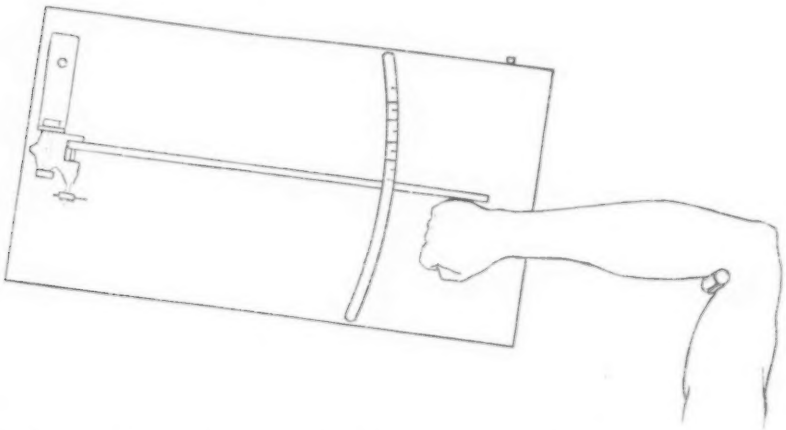


FIG. 1.—A drawing of the apparatus used for controlling muscle tension during active contractions : described in the text.

tends above the length of the brass plate but is free from contact with it. When a pressure is made in a horizontal direction against its free end it bends to a degree determined by its rigidity and the force exerted. As it yields, it passes beneath a brass arc supported horizontally upon two pillars, one at each side of the base. This arc carries upon its flat upper surface a scale indicating the various degrees of deformity of the spring. The scale is calibrated in terms of grammes and kilogrammes pressure by clamping the base plate vertically and hanging weights from the free end, the plate being clamped on each occasion at such an angle that the pull is perpendicular to the surface of the free end of the spring.

When in use the base is bolted through the table at one point near

the fixed clamp or vice; it is supported in the direction in which the force against the spring tends to make it turn by a movable stop which can be adjusted so that the base and the scale which it carries are in such a position that the spring, at its free end, is approximately perpendicular to the direction of the push which maintains it at each required degree of deformity. This adjustment, taken together with the method of scale-calibration just described, ensures that comparable measurements are being made of the push exerted by the contracting muscle in every case.

By this adjustment of the base-plate and by substituting different laminar springs, for each of which the scale is calibrated anew, the apparatus may be made to resist any desired force exerted by the muscle in a constant direction.

The scale is illuminated by a small electric lamp run from a dry battery and is viewed by the subject through a mirror and a large hand lens, each supported upon the table. When a particular tension is re-

FIG. 2.—A drawing of the concentric muscle electrode, after Adrian and Bronk [1] (modified).

quired in the extensors of the fore-arm, he is directed to push against the spring until its upper edge appears to coincide with a corresponding mark on the scale. The position of the base is then adjusted so that this pressure can be maintained with the arm and fore-arm at right angles with each other. A progressive change of tension may be recorded either approximately, by getting the subject to push the spring gradually across the scale, or more exactly by getting him to resist its increasing elastic restoring force as the base is uniformly moved so that the deformation of the spring is increased.

The electrode. (Fig. 2).—This is of the needle type described by Adrian and Bronk [1]. For the records here described it was made in the following way. A length of No. 36 enamelled wire was pushed through the lumen of a hypodermic needle 3·5 cm. long, to the base of which a stout piece of silk-covered wire has been soldered. The needle was then fitted on to the nozzle of a 10-c.c. syringe with the enamelled wire passing up into its barrel. Some paraffin wax was put into the syringe beneath the piston and the whole placed in an incubator until

the wax was melted. Pushing down the piston then carried the wax along the enclosed wire through the needle, so that when the whole was allowed to cool the central electrode was insulated by both its enamel covering and by the paraffin wax which otherwise filled the lumen and base of the needle. In those cases in which this had been successful the wire was at one end cut off short at the tip of the needle and at the other wound twice round its base and secured with a strip of adhesive tape. The insulation, and the presence of an exposed surface just short of the needle's point, were tested with a battery and lamp before using.

The needle was pushed into the outer side of the arm at a spot where palpation readily revealed a local swelling and hardening of the triceps muscle with voluntary effort. The skin was treated first with tincture of iodine which was allowed to dry; through it the needle could always be thrust without more than negligible discomfort. The needles were kept in pure lysol, and immediately before use were wiped over with 2 per cent. lysol.

The amplifying apparatus.—This is the standard amplifying unit supplied by the Clifton Instrument Company for use with the Matthews' Oscillograph, and was used in accordance with the directions advised by them. The boxes of valves and batteries necessary for their use will not be described in detail. The lead from the hypodermic needle itself was connected to the negative input of the first box of valves—this side of the circuit being earthed. That from the electrode was connected to the positive terminal of the input.

Only three of the four amplifying valves in cascade were used for obtaining these records, and with these the rheostat control had to be adjusted so that their effect was never maximal. The first box, although padded inside, had to be further protected by being stood upon rubber matting and covered with cotton-wool blanketing—without this the auditory vibrations from the loud speaker were sufficient to set up "howling" and oscillation with any but minimal amplification.

Of the final four valves, three were led off to the coils around the oscillograph, and the fourth was connected with the loud speaker. A special cable and terminal block were supplied for this purpose.

The recording apparatus.—A pointolite lamp was focused upon the mirror of the oscillograph and its light reflected on to the aperture of a moving film camera 5 m. distant, where a circular field of illumination was cast 20 cm. in diameter. The shadow of a vertical bar placed between the lamp and the oscillograph was cast upon the camera. The record obtained consisted of the horizontal movements of the edge of this vertical shadow.

To avoid mechanical vibrations both the oscillograph and the vertical bar were stood upon heavy iron stands provided with fine vertical adjusting screws and having tripod bases. Each foot of the base was supported upon the bottom of an upturned crucible resting upon a thick layer of "Sorbo" rubber matting. In this way it was found possible to eliminate all noticeable mechanical vibrations except those set up by a heavy blow upon the bench which carried the tripods, and in the absence of any electrical variation the base line was clear-cut and linear.

Time intervals were recorded upon the film by allowing the prong of an electrically-driven tuning fork to intercept the light at one edge.

Apparatus for the graphical recording of arm movements. (Fig. 3).—

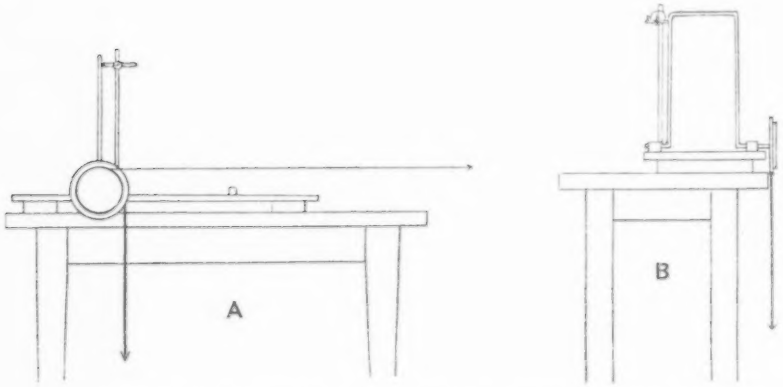


FIG. 3.—A drawing of the apparatus used for graphical recording of active and passive movements of the fore-arm. *A*, lateral view: *B*, end-on view. Described in text.

A piece of iron bar bent into a rectangular framework is supported at each end upon lubricated bearings clamped at either side of a narrow wooden board. One end passes some distance beyond the bearing and serves as the axle for a rigidly attached pulley wheel. This wheel is made up of a number of discs of differing diameters each grooved at its circumference. A steel cable which supports a heavy weight passes over the edge of the largest pulley disc and is tied on to the axle. A fine stout thread is used to connect one of the other pulley discs to the kymograph, that disc being chosen which gives the most convenient size of record. As the framework is rotated about its bearings the weight is raised or lowered and the recording thread is wound on to or off the pulley.

A vertical support screwed into the same board carries at its upper end a horizontally hinged bar which can be made to engage with the rotating framework above. It may be used as a stop to hold this in the vertical position against the force exerted by the hanging weight. A similar stop is fixed further along the board in such a position that it can hold the framework down in the horizontal position against the weight when this is so directed around the pulley that it tends to bring it into the vertical.

When the stop which is temporarily acting as a support is suddenly removed, the framework rotates through a quadrant and is arrested in the case of upward movement by the other stop, in the case of downward movement by a rubber buffer glued on to the wooden base. A soft pad acts as a comfortable rest for the elbow. The table is at such a height that a patient sitting upon a chair at its side can rest his elbow upon the pad with his upper arm at 45° with the horizontal. The pad raises the elbow so that the axis of rotation of this joint coincides with that of the framework. The fore-arm rises vertically from the elbow-joint with the shoulder externally rotated, and in this position the wrist rests against the middle of the framework when this is held by the upper stop. The wrist is fixed to the bar at this point by means of a padded leather strap.

In this way the fore-arm can be made to lie in the plane of the rectangular framework and to follow it passively or to move it actively, the force between the arm and the frame being at all stages of movement directed perpendicular to the arm at a constant distance from the elbow. The angle between the fore-arm and upper-arm varies between 45° and 135°.

The records obtained are those of flexion and extension at the elbow-joint, not of shortening and lengthening of any particular muscle. As it was the form of movement which was chiefly being investigated this was considered not to be a disadvantage. Where rigidity or resistance to passive movements is being recorded no inference can be drawn as to any relation between the resistance offered by the muscles and their degree of lengthening.

The apparatus was used for three different types of record, those showing :—

(i) Rigidity, as resistance to passive movement.

(ii) The continuous or discontinuous character of the voluntary movements.

(iii) The maximum rate of voluntary movements.

The results of measurements of rigidity and of the maximum rate of movement form the subject of another paper in course of preparation. The form of the slow voluntary movements alone is here considered.

The continuity of voluntary movements was recorded by directing the subject gradually and uniformly to flex and then to extend his forearm. The efforts could be made with the framework unloaded or loaded with any desired weight pulling in the direction of either flexion or of extension. The records here shown were all obtained as efforts at uniform contraction and relaxation of the fore-arm flexors against a steady couple tending to produce extension.

For the routine recording of voluntary movements the loading of the apparatus was arranged so that normal subjects were able to carry out gradual flexion and extension of the fore-arm yielding curves which showed no break in the general smoothness. This was necessary because when the load is very much increased so that these movements require all the strength which the subject can exert, even normal persons show an intermittency of contraction recorded as curves showing the same steppage effect as is shown by Parkinsonian patients when much less effort is being made.

The results.—When the electrode-bearing needle is inserted into the triceps of a normal subject whose arm, fully supported upon a horizontal surface, is in complete voluntary relaxation, no disturbances are audible in the loud-speaker and none are recorded upon the oscillograph tracing.

When the needle is similarly inserted into a paralysis agitans patient the same obtains in the absence of visible or palpable tremor.

However, when tremor is sufficiently active, there is received from the loud-speaker a series of sounds each resembling a brisk "rumble," and each repeated at regular intervals in a rhythmical series completely synchronous as far as the ear can detect with the tremulous excursions of the arm from which the lead is taken. At the same time deflections of the oscillograph beam occur which, when photographed, show that each tremor contraction of the muscle corresponds to an outburst of activity such as would be expected if a volley of impulses was arriving at rhythmically spaced intervals, the rhythm being identical with that which may be graphically recorded from the limb segment moved. Such records have the general appearance shown in fig. 4.

When a normal subject, into whose triceps muscle an electrode-bearing needle has been inserted, attempts to extend his elbow against some comparatively immovable support the previously silent loud-speaker and quiescent oscillograph become active, a series of sounds is received

from the former and a series of deflections appear in the latter. These have been already described by Adrian and Bronk [1]. If the subject attempts to maintain in his triceps just sufficient minimal active tension for producing a constant stream of sounds from the loud-speaker, the camera records a series of deflections from the oscillograph of equal height and occasionally of regular rhythm or rhythms (fig. 5). As the tension is progressively increased the record (fig. 6*a*) shows, in the early stages of this increase, the addition of other series of regularly spaced deflections, each series appearing at no definite phase interval with relation to the other series already present. A stage is soon reached (fig. 6*b*) at which the deflections increase considerably in average amplitude and at the same time occur so frequently, with such varying degrees of overlap and summation that regular series are no longer with certainty detectable, although a measurement of the total number occurring per second shows that this continues to increase as the tension rises.

When the effort is very greatly increased and the active tension developed in the muscle becomes very large, there appears in all normal persons a tremulous maintenance of this tension. If the muscle is pulling against a strong spring, the slight distortion of which may be used to give a record of isometric muscle contractions, it is found that the tension fluctuates partly regularly and partly irregularly about the level at which an effort is being made to maintain it. A tremulous graphical record such as this may be obtained simultaneously with a deflection record from the oscillograph (fig. 7) which shows that there are outbursts of discharge alternating with periods of comparative quiescence. The frequency of these outbursts is identical with that of the tremulous graphical record. Such an oscillograph record suggests that in these circumstances the deflections are grouped together at intervals and are provided by discharges from within the muscle which, instead of being quite irregular in size and aperiodic, are volleyed from the muscle in groups of comparable amplitude.

When the experiment is repeated with a paralysis agitans patient substituted for the normal subject certain differences in the oscillograph records and loud-speaker sounds are noticed.

Discharges of low frequency and regularity both as regards amplitude and spacing are comparatively rare. Either such response at minimal active muscle tension are uncommon or else such patients show a greater difficulty in achieving and in maintaining such slight degrees of activation of their muscles.

The deflections tend to occur, both at low and at high frequency, in groups. These groups may be either wholly irregularly, or in part regularly, spaced. They occur in nearly all such patients when the tension developed is considerable and may show this phenomenon of grouping or volleying of the discharge at quite low tensions. The patients in whom the volleying is best marked at higher tensions are those in whom it appears also at the lowest degree of tension development and becomes progressively more obvious as this is increased (fig. 8).

Such volleying is always maximal while a constant active tension is being maintained at any particular level. If the muscle tension, after being kept constant along one level, is progressively increased to a higher level at which it is then again kept constant, the volleying of the discharge, well-marked at the constantly maintained lower level, tends to disappear while the tension is increasing and to reappear at the maintained higher level (fig. 9). During the phase of tension-increase the oscillograph record bears a much closer resemblance to those of normal subjects, i.e., the deflections are all out of step one with the other and of widely differing heights owing to fortuitous overlap and summation.

Interpretation and Discussion.

When the needle carrying an electrode is inserted into the muscle of either a normal subject or a paralysis agitans patient an electrical discharge can be recorded only if the muscle is

(i) being actually contracted,

(ii) engaged in visible and palpable tremor.

This suggests that the discharge recorded is associated in some way with voluntary or involuntary muscle activity.

If the muscle, while voluntarily relaxed and not showing tremor, is passively stretched and allowed to shorten again, gross changes in the base line of the oscillograph record are obtained (fig. 12), but none of the quick deflections typically associated with muscular activity. Such gross changes may be put down to shifting of the electrode within the substance of the muscle.

It has yet to be decided whether the quick deflections met with during activity of the muscle, either voluntary or involuntary, are due to such mechanical alterations in the relative position of the muscle and of the electrode occurring at a much higher rate, or to that activity of the muscle fibres which provides the development of tension, i.e., the tendency to contract.

The quick deflections occur not only when the muscle is shortening or lengthening but also when it is being kept at a constant tension. If they are due to mechanical shifting of the electrode at a very rapid rate it follows that there must be relative movements of the fibres or groups of fibres within the muscle if not of the whole muscle itself. In the case in which the whole muscle is maintained at a constant length the relative movements of its parts must be summing in such a way that the shortening effect of those fibres which are contracting is at any instant exactly counterbalanced by the lengthening effect of those which are relaxing.

We know that when a muscle is stimulated by a break shock from an induction-coil delivered over its "motor point" it responds by shortening and then relaxing. This sudden twitch of the muscle is provided by the simultaneous stimulation of a number of motor neurones and the simultaneous activity of many muscle fibres. If a series of such stimuli are provided at an increasing, regular frequency, the muscle relaxes less and less completely after each contraction until a stage is reached at which shortening is maintained and no relaxation can be seen to occur. At this point an increase in the strength of the stimuli supplied leads to a raising of the level at which tetanus is occurring but does not lead to any breaking up of the tetanic plateau.

Since an artificial stimulus of this nature throws into activity a number of muscle fibre units, perhaps with different intensities according to their accessibility to the stimulus, but each at the same instant, the total amount of shortening shown by the muscle must be equal to the sum of the shortening of its separate parts.

If a regular series of such stimuli in rapid succession are delivered, the muscle fibres which are in any measure activated will continue to contract and relax together provided their refractory periods do not widely differ. Therefore if such a series produces maintained shortening of the muscle as a whole, it follows that it must be occurring at such a rate that the muscle fibres themselves do not relax in between the stimuli but remain each in a state of maintained contraction. Yet the oscillograph continues (fig. 10) to show a series of deflections synchronous with the stimuli coming from the muscle fibres. Therefore in these circumstances, at least, the electrical changes recorded must be due to the constant contractile activity of the muscle fibres and not merely to shifting of the electrode within the muscle.

When a muscle is maintained by voluntary effort in a state of steady tension there is probably some rotation of activity amongst its fibres, and

it is not suggested that the same fibres are always called into play and remain contracted to provide any one degree of shortening. But it is suggested that the fibres which are at any one moment keeping the muscle in a state of steady contraction are themselves all in a condition of maintained shortening (apart from those few which may be actually falling out of, or coming in to, activity in course of rotation). If this be so, then the deflections recorded in this case also must be referred to the contraction process itself and not to mechanical shifting of the muscle fibres beneath that part of the electrode.

Some light is also thrown upon this explanation by the results of leading from animal muscle-nerve preparations. If the tendo Achillis be freed from its insertion into the calcaneus and pulled upon, from a needle electrode placed into either the soleus or the gastrocnemius, deflections are set up in the galvanometer of a slow type, mounting while the pull operates and falling while it is being released.

If the sciatic nerve trunk is dissected out and stimulated with repeated break shocks, the contractions of the soleus and gastrocnemius may be registered graphically through the tendo Achillis. For each contraction a deflection can be received from the oscillograph with the electrode placed in either muscle. Each stimulus gives rise to a single contraction and a single oscillograph deflection (fig. 10). Each deflection might be regarded as being due to the alteration of length of the muscles at each contraction, its much more abrupt form being the result of an active change of shape which is much more rapid than that which can be passively produced by pulling upon the tendon.

The observations show that this is in fact not a reasonable explanation for these deflections.

When the muscle is tetanized into a state of maintained shortening the electrical disturbances continue to follow accurately the rate of stimulation as described above.

When the two heads of the gastrocnemius muscle are left attached to the same tendon and the nerve supply to one of them, e.g., the lateral head, is cut, stimulation of the sciatic trunk is followed by deflection of the oscillograph only when the needle is in contact with that part of the muscle to which the nerve supply is intact, in this case the medial head. Yet the lateral head being still attached to the same tendon moves, without contracting, with each alteration of length of the medial head. No deflections can be recorded from it as a result of stimulation of the sciatic nerve, but the typical slow shifts of the base line still occur when the tendo Achillis is passively pulled upon.

The slow shifts of the base line produced by passive movements whether in animals or in man are in one direction only, i.e., they resemble long drawn out monophasic responses (fig. 11). The deflections described as associated with active contraction of the muscle fibres are displasic in form.

It therefore seems highly probable that the deflections recorded from human subjects in the way above described are the result of electrical changes within the muscle associated with the contractile activities of its fibres.

If we seek to interpret the records obtained from normal persons we have to bear in mind the following observations:—

(1) At low tensions voluntarily maintained the discharge consists of one or more regularly spaced series of disturbances.

(2) At low tensions also the size of these disturbances shows a remarkable constancy both as regards different series and as regards the individual members of any one series.

(3) Where overlapping of such disturbances from different series occurs they summate to give a deflection of increased height.

(4) When the tension is increased the total number of disturbances at first increases, while the series in which they occur remain completely out of step and they remain of approximately unaltered size.

(5) As the tension is still further raised a stage is reached at which the deflections are all of much increased amplitude but are still quite irregularly spaced.

(6) When the tension is finally raised to near its maximum the deflections tend to be thrown together into groups and the discharge from the muscle occurs in volleys. This stage corresponds to the development of tremulous effort in the graphical records of muscle tension.

It is, therefore, suggested that the regular series of infrequent deflections of equal and small amplitude, which can, with facility, be obtained from most normal persons when assisted by the help of the loud-speaker sounds as a control upon their effort output, is produced by a series of regularly spaced and equal discharges from the muscle, originating in the action currents furnished by outbursts of activity in some small unit of the muscle in the immediate neighbourhood of the electrode. Those small units may be either single muscle fibres or else

groups of two or three fibres which are normally always activated simultaneously as a unit.

The fact that the size of the deflections varies imperceptibly from series to series at such minimal tensions, suggests that the units activated on such occasions all consist of about the same number of muscle fibres.

It is possible that the rate of discharge from such units during minimal contraction of the muscle is not the greatest of which they are capable and that therefore the interruption of one rhythm and the substitution of another or of a series of aperiodic deflections cannot necessarily be ascribed to the switching over from one unit to another.

Also the deflections caused by discharges of equal size, but taking place from units at different distances from, or differently related to, the electrode will not themselves be equal.

Therefore it is probable that a series of deflections of identical amplitude are set up by action currents occurring in the same muscle unit.

When the tension within the muscle is voluntarily increased each unit begins to fire off more rapidly and other units come into operation. While the occasional occurrence of a deflection of greater amplitude at low tensions may be reasonably regarded as due to the chance overlap of discharge from different units, the records from muscles at higher tensions in which the deflections are all of much greater amplitude cannot reasonably be so explained, and it is suggested that at such increased tensions a progressive fusion of several units into synchronously operated larger groups takes place—the discharge from these being in all cases greater.

As the tension is still further increased this process of synchronization of smaller units into larger groups continues and is at first complete as far as the records here obtained can show, i.e., the larger deflections show no sign, as far as their geometrical form is concerned, of their complexity of origin from different units. There is, however, evidently a limit to this completeness of fusion, i.e , a limit to the number of units which can be simultaneously activated, and the synchronism, complete for small groups, is only partial for larger groups, and the discharges, not falling exactly simultaneously, provide those volleys which are characteristic of the maximal tensions.

It is possible that this limit is not a function of the muscle fibres but one imposed by the neuronic connections either in the peripheral nervous pathway or at a higher level. This, however, is a speculation which further experiments must investigate.

Another observation not previously here mentioned supports this line of explanation. It is that when, during slight voluntary activation of a muscle such as the triceps, involuntary fibrillation of the muscle occurs, each twitch of that part of the muscle belly into which the electrode needle is inserted is accompanied by an extra loud "pop" from the loud-speaker and an abnormally large deflection upon the record (fig. 13). Here at least we have evidence of the simultaneous discharge of a large group of muscle fibres in the immediate neighbourhood of the electrode which raises a visible knot upon the surface of the muscle and initiates a discharge of increased size comparable to those obtained from the same muscle at much higher degrees of voluntary activation.

In all cases in the course of this work in which electrical records have been obtained from muscles in active contraction, shortening has not been permitted to any extent. The disturbances of movement shown by patients suffering from paralysis agitans on the other hand necessarily appear with the muscle in approximately isotonic activity. In attempting to explain these clinical findings in terms of experimental results this difference demands attention. We know from the work of Adrian that afferent impulses arising in a muscle during its contraction do influence the discharge of motor efferents to that same muscle when the preparation is for these purposes intact, and it is therefore possible that the volleying of such efferent impulses which we have found to be characteristic of sustained isometric contractions in paralysis agitans patients may be influenced by afferents from the muscle which are not similarly active when the muscle contracts isotonically and movement of the limb segments is permitted.

It is extremely improbable, however, that the whole effect is contributed entirely by the isometric conditions of recording the tension development. Thus the tremor records from a limb in voluntary relaxation showed shifts of the base line associated with the tremulous excursions of the limb and also typical action current deflections which are characteristically volleyed. Further, those patients whose electrical records show a well-marked tendency to volleying all yield a tremulous graphical record of active flexion and extension.

Therefore it seems reasonable to suppose that just as constant active maintenance of tension within the muscle depends upon a relative asynchronism of activation of the muscle elements, so also does the ease with which gradual changes in length of the muscle are provided or permitted by contraction or relaxation, and hence the smooth execution of voluntary movements, depend upon the same factor.

That the tremulous character of voluntary movements shown by patients suffering from paralysis agitans is due to a disturbance of this relative asynchronism seems a reasonable explanation. The suggestions that this phenomenon of dynamic tremor or step-like contraction and relaxation is due to intermittency of voluntary effort, to faulty and intermittent relaxation of movement antagonists or to the disturbing effect of some hypothetical "tremor centre," are all extremely unsatisfactory. The steppage of voluntary movement occurs at a rate which is far higher than that which might be explained in terms of spasmodic voluntary effort. Defective relaxation of the antagonists, even if otherwise satisfactory as an explanation, could apply only to disturbances of limb movements in which shortening and lengthening, or vice versa, respectively of the two muscle groups were permitted, whereas we know that intermittency of effect is more readily observed under conditions of isometric activity. Further, this explanation of faulty relaxation of antagonists argues a defect of co-ordination and reciprocal innervation which is not shown in any other conditions of movement and must be arbitrarily held to be restricted to the mutual relations of muscles acting in opposition upon the same limb segment. Moreover, the graphical records show that during, for example, active flexion and extension of the elbow against a constant force tending to cause extension, the tremulous character of the movement record is present both during contraction and during relaxation of the flexors, and that where any obvious difference in the degree of this dynamic tremor is present (apart from the sudden temporary yield which occurs at the switch-over from contraction to relaxation) it is better marked during relaxation than during contraction. If the steppage of active contractions is to be explained as due to defective co-ordination between the flexors and extensors and allied to the motor perseveration with fixed retention of posture seen elsewhere in these patients, it would be expected that in the above circumstances flexion would be much more tremulous than extension. For during flexion the retention of shortening in the extensors would considerably hamper the efforts of the flexors, while during extension the tendency of the triceps to remain lengthened could not possibly affect the smoothness of this movement which is dependent entirely upon relaxation of the flexors yielding to the constant passive force tending to produce extension.

The implication of some hypothetical tremor centre as being responsible for both the static tremor and dynamic tremor of voluntary movements bears no relation to the observed facts and introduces an unnecessary complication.

Since the earliest description of the static tremor of paralysis agitans it has been recognized that this characteristically disappears temporarily when the relative position of the limb segments is altered and reappears when they are again relatively fixed—this reappearance does not take place at once, but only after a short period of quiescence, after which it increases to its original degree.

This observation is clearly allied to the results of electrical recording here reported, inasmuch as the volleying of action current discharge which is seen at any one degree of maintained tension disappears as the tension is increased and reappears when the tension is again kept constant at another level, i.e., the volleying is either only present, or if otherwise present is maximal when the total activation of the muscle is constant, and absent or minimal when it is changing.

It is noteworthy that this transitory asynchronism which accompanies changes of tension in the muscle and which contrasts with the abnormal synchronism associated with maintained contractions, is characteristic of changes made in the directions of increase and not of decrease of activity.

This suggests that while the tension is increasing new units are thrown into activity in the normal way, i.e., out of phase with those already in operation, that when the tension is kept constant the impulses tend to be thrown into progressive synchronism, and that during decrease of the tension the volleying of impulses does not disappear in the same way as during its increase because the activated groups are allowed to fall out of activity as groups, i.e., the individual units are not dissected out from the groups into which they have been thrown and allowed to become inactive separately. If this be so, then the fact that increase of tension is achieved through the activation of further units, while decrease of tension is brought about by the successive damping down of synchronous groups, accounts for the observations recorded above that the shortening of a muscle in opposition to a constant force is more smooth than its lengthening when yielding to the same force.

Some degree of synchronism of motor units is normal in healthy subjects under certain conditions which have been detailed above. Higher degrees of synchronism appear under maximal voluntary effort, when these are sustained for a period which leads to rapid fatigue. Complete synchronism is only found in the tendon reflexes (fig. 14) and in the muscle-twitch artificially evoked by electrical stimulation of the muscle at its motor point.

Patients suffering from paralysis agitans show a tendency towards

abnormally high degrees of synchronism of the voluntarily activated motor units. This provides the difficulty in grading fine or slow movements and the difficulty in maintaining constant tensions seen in such cases. It has been shown that involuntary tremor is associated with a volleying discharge of motor units of the same type as that shown in voluntary movements.

To Professor Adrian, who very kindly advised me in the setting up of the apparatus and of whose work this is an application, my sincere thanks are due. I have also to thank the physicians of University College Hospital and of the Hospital for Epilepsy and Paralysis, Maida Vale, for allowing me to have free access to their cases of Paralysis Agitans for the purpose of this investigation.

REFERENCES.

[1] Adrian, E. D. and Bronk. *Journ. of Physiol.*, 1929, **67**, 120.
[2] Matthews, B. W. C. *Ibid.*, 1928, **65**, 225.
[3] Schafer. "Textbook of Physiol.," Edinburgh, 1900, **11**, 207.
[4] Walshe, F. M. R. Oliver Sharpey Lectures. *Lancet*, 1929, **1**, 1024.

LEGENDS TO FIGURES.—PLATES XXV-XXVIII.

Fig. 4.—Records taken electrically from the right triceps muscle of a woman suffering from paralysis agitans. The arm is being fully supported and relaxed as much as possible. Tremor was easily visible at the rate of 100 beats in 18 secs. The time marker (below) records 1/100 secs.

Fig. 5.—Record taken from the right triceps muscle of a healthy normal subject, during a minimal voluntary extension effort controlled by the loud-speaker sounds. Time intervals (below) 1/100 secs.

Fig. 6.—Three records taken from the same healthy normal subject as in fig. 5. They show three stages in the steady increase of active contraction. Time marker below 1/100 secs.

Fig. 7.—Record taken from the right triceps muscle of the same subject as in fig. 5 and 6 during maximum efforts to maintain the tensometer spring as fully deformed as possible.

Fig. 8.—Record taken from the right triceps muscle of a man suffering from paralysis agitans during his effort to maintain a steady active contraction of minimal force.

Fig. 9.—Record from a Parkinsonian patient. During the early part of the record the patient was maintaining a steady contraction equivalent to a push against the tensometer of 3 kgm. This was then gradually increased to a push of 5 kgm. and again kept constant at this level. It shows that the volleying present at the lower level of steady tension disappeared during the stage of increasing tension and reappeared when it was again kept constant at a higher level.

Fig. 10.—Reproductions of graphical and electrical records obtained simultaneously from a rabbit. The electrical records were those from a needle electrode pushed into the right soleus muscle. The graphical records were obtained from an isometric torsion spring myograph connected to the tendo Achillis detached from its insertion. The graphical records marked 1, 2, 3, 4 contain each three lines. The lowest indicates break shocks supplied to the exposed right sciatic nerve-trunk from an induction coil. The middle line indicates time intervals of 1/5 sec. The uppermost line is the myographic record. The rate of stimulation was increased by steps from records 1 to 4 : being constant throughout any one record.

PLATE XXV.

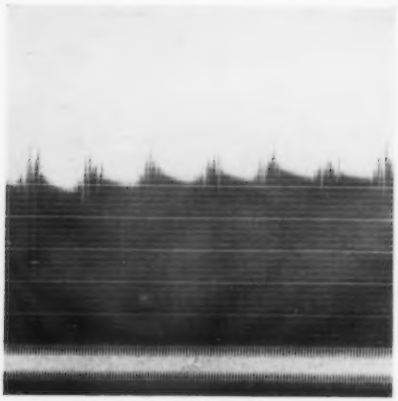


FIG. 4.

FIG. 5.

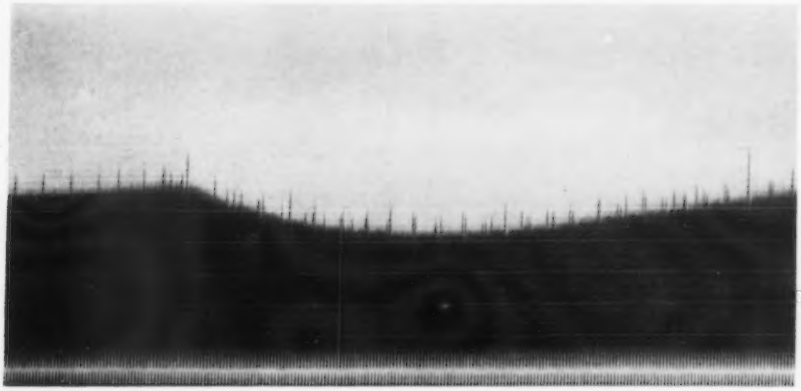


FIG. 6*a*.

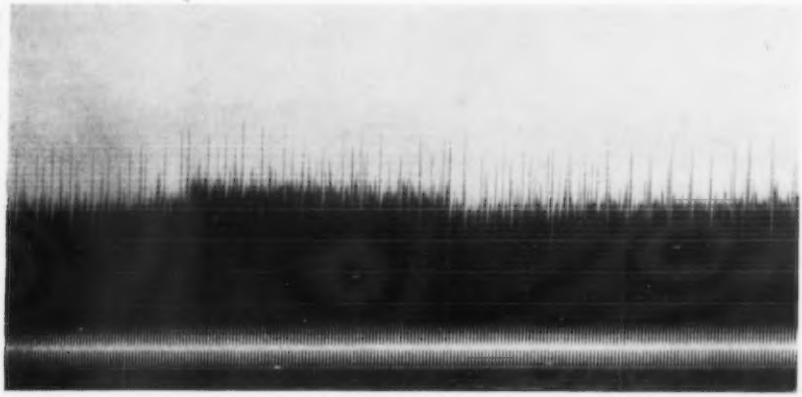


FIG. 6*b*.

PLATE XXVI.

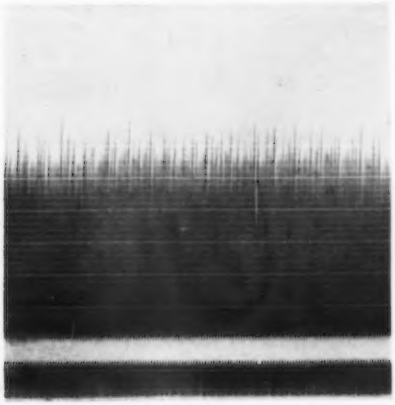


FIG. 6c.

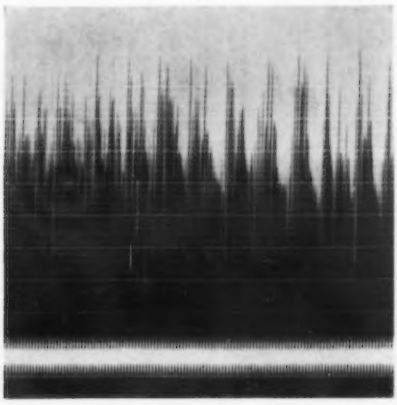


FIG. 7.

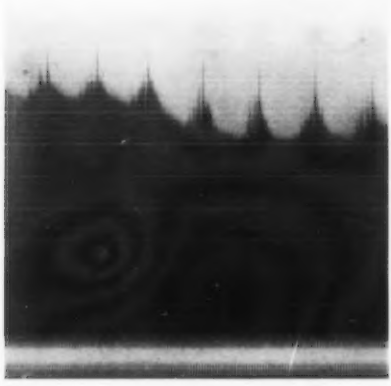


FIG. 8.

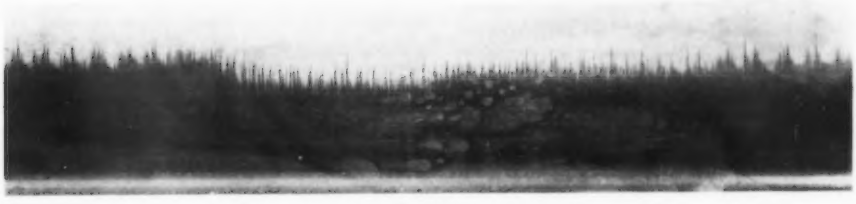


FIG. 9.

PLATE XXVII.

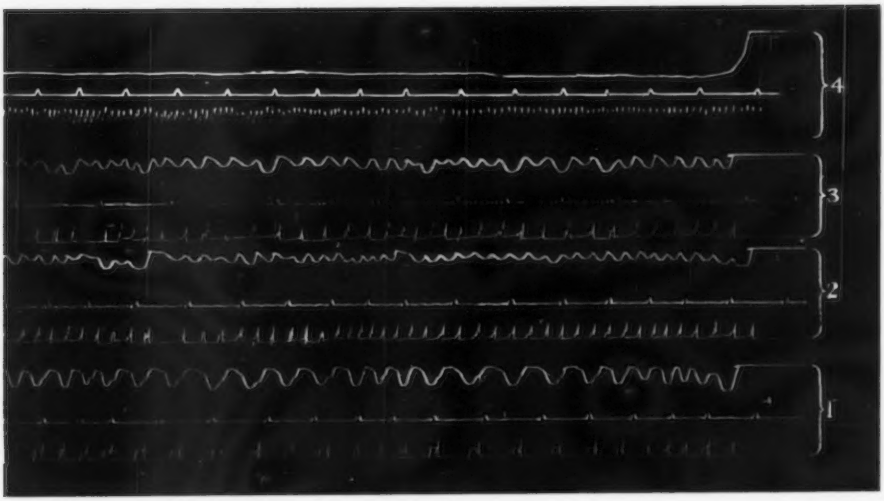


FIG. 10*a*.

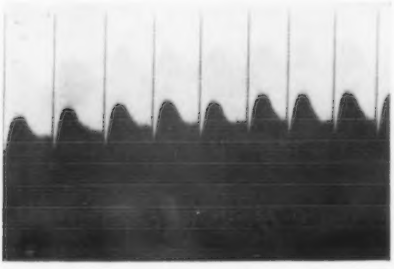


FIG. 10*b*.

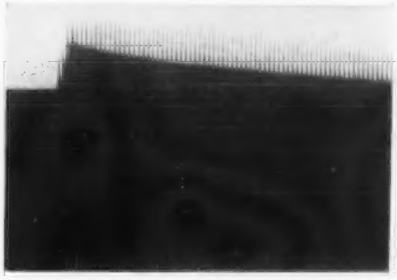


FIG. 10*c*.

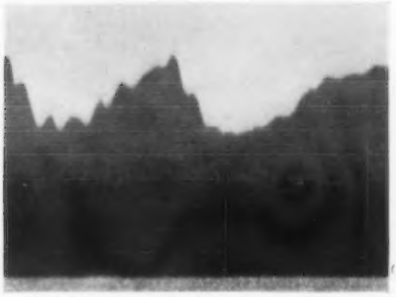


FIG. 11.

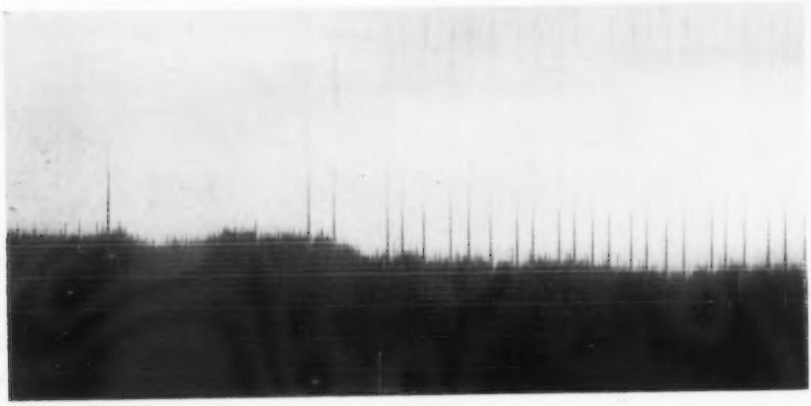


FIG. 12.

FIG. 13*a*.

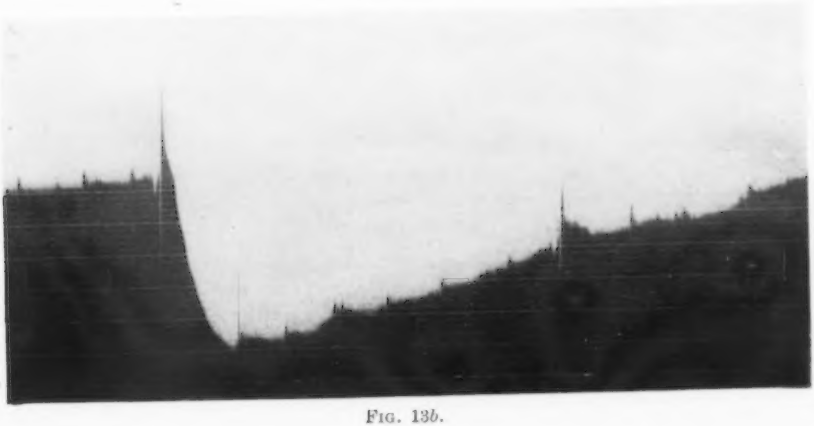


FIG. 13*b*.

The electrical records accompanying these bear the same numbers as the graphical records to which they correspond. It will be noticed that at low frequency each stimulus gives rise to a contraction-relaxation wave in the graphical record, and an action current deflection followed by a shift of the base line due to slight muscle shortening, in the electrical record. At high frequency the graphical contractions have fused into a tetanus without relaxation, but each stimulus is still followed by an action current in the steadily contracted muscle.

FIG. 11.—Record taken from the triceps muscle of a patient with paralysis agitans. The arm was fully supported and complete voluntary relaxation requested. Passive flexion and extension of the elbow gave rise to the gross shifts of the base line here recorded, in which is seen the cogwheel type of resistance to such passive movements.

FIG. 12.—Record taken from the triceps muscle of a normal healthy person during slight voluntary contraction effort. The muscle showed fibrillation of that part of its substance impaled by the needle. The very large deflections seen on this record occurred simultaneously with visible local fibrillation of the muscle.

FIG. 13.—Records taken from the soleus muscle of a patient suffering from paralysis agitans. During the upper record voluntary relaxation was complete—during the lower record a slight contraction effort was being made. The tendo Achillis was tapped with a tendon hammer twice during each record. The upper record shows the sudden action current. This followed a slight downward deflection of the base line due to the tap and was followed by the grosser changes due to the muscle shortening. The lower record shows two large action currents each preceded by a downward shift of the base line due to the tap on the tendon. Each sudden synchronisation of the action currents provided by the tendon reflex is followed by a short period of inhibition. The first gave rise to a visible reflex contraction, and some activity rebound is seen upon the record. The second did not set up any visible reflex contraction but the action current, the inhibition and the slight rebound are all present.

Proceedings of the Section of Neurology of the Royal Society of Medicine.

President—Dr. Gordon Holmes, C.M.G.

Clinical Meeting held at the National Hospital, Queen Square, W.C.1, on Thursday, November 14.

Chronic Abscess of the Spinal Cord.

By Macdonald Critchley.

Female, aged 18. Two and a half years ago had a septic arm requiring three operations. Four weeks afterwards had an attack of headache, backache, vomiting and fever, lasting about thirty-six hours. From this time similar attacks recurred with great regularity every nine days. Six months later was admitted to a general hospital where she remained under observation for over six months. A tentative diagnosis of rat-bite fever was made. The attacks gradually decreased until Easter, 1929, when after a particularly severe bout the legs became weak. This was actually the last febrile attack, but weakness of the legs persisted and grew progressively worse. Gradually numbness of the lower limbs, constant pain in the back and loss of sphincter control developed. On examination—spastic paralegia with sensory loss, up to level of sixth thoracic segment. X-ray examination of spine revealed no abnormality; lipiodol was held up between the fifth and sixth dorsal bodies. Cerebro-spinal fluid showed a well-marked loculation syndrome.

Operation, August 2, 1929 (Sir Percy Sargent).—Mid-dorsal laminectomy: in the region of the seventh dorsal spine the dura was greatly thickened. When this was incised, a mass was discovered lying outside the cord, especially on its left lateral aspect. Portions of the mass and of the overlying dura were removed for investigation. Histological examination revealed that the mass was composed of highly vascularized granulation tissue containing numerous staphylococci. The dura contained abundant infiltrations of plasma cells.

For the first three weeks after the operation there was a purulent discharge from the wound, which afterwards ceased altogether. There has been some return of movement and sensation to the legs and an obvious improvement in the general health.

Dr. P. Cloake said he was not convinced there was any relation between the original infection of the patient's arm and the condition found at operation, especially in view of the fact that the local infection preceded the development

of spinal symptoms by two years. It appeared to him more probable that if the granulation tissue removed at operation was inflammatory it was due to infection from some other source.

Dr. A. FEILING asked if any evidence of osteomyelitis of the vertebral column was found at the operation or in the X-ray plates. If the lesion found was inflammatory it appeared to him that it would most probably have spread from the neighbouring bone.

Dr. J. G. GREENFIELD said that staphylococci could be easily demonstrated in the tissue removed by the surgeon. This was a type of chronic granulation tissue and its slow growth could be naturally explained by an infection of low virulence. In view of the histological nature of the tissue it seemed to him quite probable that it had been present for a long period and had developed slowly.

Dr. G. HOLMES suggested that although the condition described was not an abscess of the spinal cord, the failure of more marked improvement by operation after removal of the compressing tissue suggested the possibility of chronic intramedullary infection too. He referred to cases published by Chiasi, Collier and Turner, and others, and pointed out that in typical cases of spinal abscess the symptoms developed rapidly and nearly always led to an early fatal termination.

Dr. CRITCHLEY referred to the rarity of spinal abscesses; in 1926, Adson and Woltman were able to collect twenty-nine cases from the literature, to which they added a personal case. All but two proved fatal. The history in the present case was unusually long, the longest history in the literature being seven months.

Progressive Ataxia in a Child associated with a Positive Blood Wassermann Reaction.

By D. DENNY-BROWN.

G. B., male, aged 4 years and 2 months, admitted to hospital for unsteadiness in gait, which had been first noticed eighteen months ago, and had slowly and gradually progressed, and unsteadiness in the arms, which had been first noticed twelve months ago and had gradually progressed.

He was an only child, the parents married five and a half years ago. There were no other pregnancies. Labour was not prolonged and forceps was not used. Breast fed. Perfectly healthy at birth and after, except for two attacks of "influenza," once two years ago, and once eighteen months ago (his mother also had influenza on each occasion). In each of these attacks he was irritable and feverish and vomited several times, but no other symptom was noticed. No convulsions had occurred. He was not late in learning to walk or to talk, and his gait was perfectly normal until the age of $2\frac{1}{2}$, when the unsteadiness was first noticed when he was chasing a dog on a garden lawn. He began to lisp slightly in speech about six months ago, but the lisp has not increased.

A month ago he said that his knees and toes ached, he was a little feverish (100° F.) and began to cough occasionally. The pains ceased the same afternoon and have not recurred. The cough continued up to the time of admission and he occasionally said his throat felt sore.

No history of any similar complaint, or of deaths in infancy.

Physical examination.—Bright, intelligent child, with head a little larger than normal. No stigmata of congenital syphilis. Colour good. Speech occasionally slightly lisping. Well behaved, clean in habits. Occasional dry cough with salivation. No defect in visual acuity and no defect in the fields can be demonstrated. Slight pallor of both discs, maculæ normal. Pupils react briskly to light. Diplopia on looking to extreme left and slight deficiency in outward movement of left eye. Nystagmus on looking fully to either side, fine and rapid to right, slow and coarse to left. No defect in remaining cranial nerves.

No paralysis or paresis in any limb or trunk movement, but the limbs are all hypotonic and ataxic, with some coarse irregular action tremor in the upper limbs. No wasting. No involuntary movements. Tendon jerks all absent. Abdominal reflexes present and equal on both sides. Plantar reflexes both flexor. No sensory defect to pin prick, cotton wool, heat and cold could be demonstrated. Gait is extremely ataxic and station very unsteady with eyes open. Nasopharynx inflamed, but no membrane. Culture from throat swab gave chiefly streptococci; no Klebs-Loeffler bacilli; marked reaction to Schick test.

Cerebro-spinal fluid (October 22, 1929) clear, colourless, no cells seen. Total protein 0·025 per cent.; globulin tests, negative. Lange: no change in any tube. Wassermann reaction, negative.

Blood: Wassermann reaction, positive 3,300 (October 22, 1929), test repeated (October 29, 1929) with same result.

Skiagram shows skull of hydrocephalic type but with no other abnormality.

Blood Wassermann reaction of patient's mother is negative; his father is not in England.

Antisyphilitic treatment has so far brought about no improvement.

Dr. G. Holmes said the chief interest of the case is the origin and the nature of the ataxia. The type of the inco-ordination of movement, the presence of nystagmus, the absence of sensory disturbances and the hypotonia of the limbs, all indicate that the cerebellum is involved, while the size of the child's head and the skiagrams show that a considerable degree of hydrocephalus is present. The pallor of the optic discs may be also due to this. It seems more probable, therefore, that there is a local cerebellar lesion than a diffuse atrophy, and that by interfering with the escape of cerebro-spinal fluid through the fourth ventricle it has caused the hydrocephalus. Though there has been no headache a slowly growing tumour in the vermis of the cerebellum extending into the fourth ventricle is probable; this would also explain the absence of the tendon jerks. Although the Wassermann reaction is positive a syphilitic lesion is improbable, especially as the cerebro-spinal fluid is normal.

Jacksonian Epilepsy provoked by Stimulus to Right Foot or Right Ear.

By D. Denny Brown.

A. P., female, aged 51, admitted to hospital on account of attacks of twitching of right side followed by unconsciousness. These attacks first began eight months ago.

She had suffered with no previous illnesses of any kind. Menstruation ceased at age of 48 years. Nothing pertinent in family history.

The first attack occurred in March, 1929. There was sudden unconsciousness without warning, lasting an hour, and followed by general weakness, misty vision and aphasia; gradual recovery set in and was complete in two weeks. Three weeks later she began to have attacks of unconsciousness preceded by twitching in the right hand, giddiness, and a rhythmical "clicking" noise in the top of the head. These fits occurred once a day for a month and then she had treatment in bed for the following month and remained free from attacks.

At the end of May, 1929, she got up again and began to have attacks of unconsciousness whenever anything touched her right ear, or her head just behind the ear (for example, putting her spectacles on). These fits began with a twitching and tingling pain in the right side of the face and a "clicking" noise in the head. The twitching and tingling pain spread to the right hand and arm, and then to the right side and leg. She remained conscious but could not say what she wanted to say during the attack. Weakness and numbness of the right side of the body lasted from one to twelve hours after each attack. The attacks continued on alternate days until July, 1929, when they began to occur each day and were followed by unconsciousness for fifteen or twenty minutes; speech was limited to only one or two words between the attacks and there was some continual weakness of the right arm. She was admitted to Cardiff Infirmary, and the only positive findings were weakness of grasp of the right hand and ten cells per cubic millimetre in the cerebrospinal fluid. An exploration of the left parietal cortex was made (August 29, 1929). The arachnoid had a milky appearance round the superior cerebral veins, and the region of the "supra-angular gyrus" was "very soft" and "brain needles were passed in here but no fluid obtained." The osteoplastic flap was replaced.

The attacks continued (one every two days), and six weeks ago the patient began to see, without warning, a blue light immediately in front of her eyes. This occurred at intervals of two to three days, and lasted twenty minutes each time. The light came and went rhythmically with the frequency of the pulse, and had no relationship to the time of occurrence of other phenomena.

Also six weeks ago she began to have attacks of unconsciousness, brought on by some particular stimulus to the right foot or the right leg below the knee, for example pulling a stocking over this foot. These attacks also began with clicking in the head and a tingling pain and twitching starting in the

right foot and passing up the right leg, and down the right arm and to the face. They were followed by unconsciousness for a few minutes and by residual numbness, aphasia and increased weakness of right limbs for an hour or two.

For a month one or other kind of attack occurred every day, and she was afraid to touch her right ear and right foot. Once an attack was provoked no further attack was caused by touching either of these parts until about twenty-four hours had passed, and then some chance movement with contact at one or other part excited another attack.

During the last fortnight the attacks have been fewer, and she had not had one for a week previous to admission, in spite of frequent stimuli to the "sensitive" parts. Since August, 1929, she had had occasional double vision when looking to the right, lasting an hour or so. Has had frequent difficulty in remembering the names of things, and her husband's name for the last two months. She has not been able to write intelligibly since the beginning of August. She has often lately seen a large shadowy figure to her right side, but it is not there when she looks round, and she has not seen it when she looks forward again.

Physical examination.—Slight dysarthria of lingual type. Visual acuity $\frac{6}{12}$ right and left. No field defect to white or colours. Disc edges are clear, their colour is good, and the vessels of normal appearance. Variable rapid nystagmus occurs on looking to right, and slow jerks on looking to left. Hypalgesia to pin-prick over right face. Other sensations unaffected. Corneal reflexes are brisk and equal. Right palpebral fissure is wider than the left and there is weakness of the right side of her face. Palate moves slightly to left on articulation. Tongue is protruded to right. Occasionally very fine rapid tremor is present in her left hand, but there is no weakness, change in tone, or inco-ordination in either upper limb or either lower limb. Tendon reflexes are all present and equal on the two sides. The left plantar response is flexor, the right less definitely flexor, but not extensor. The abdominal reflexes are absent on both sides.

There is hypæsthesia to pin-prick and cotton wool over the whole right side, but no inaccuracy to heat and cold, no astereognosis, and two-point discrimination is equally accurate in both sides.

No bruit can be heard over any part of skull. Blood-pressure is 115/70. Gait is normal.

Cerebrospinal fluid: pressure 190 mm., three cells per cubic millimetre. Total protein 0·065 per cent., globulin tests negative. Lange, no change: Wassermann reaction, negative in cerebrospinal fluid and in blood.

Skiagrams show no calcification within skull.

Two attacks have been observed, each brought on by stimulus to the right foot, one on October 26, 1929, and one on October 31—stimulation of right foot and right ear on each other day has not provoked an attack. The first attack was produced by eliciting the knee-kerk on the right side, the second by pulling the bedclothes away from the right leg. Both attacks began by tonic

extension followed by twitching of the right ankle, knee and hip and then of the right arm, the right side of her face and immediately following this of the whole left side at once. The pupils were inactive, no bruit was heard over the skull, and no plantar responses were obtained (great toe tonically flexed). Duration of unconsciousness about four minutes, followed by aphasia and then marked perseveration, with weakness of the right arm and leg and an extensor response on right side. Complete recovery was attained three hours after onset of the attack, with return of all signs to those found on admission.

Dr. GORDON HOLMES referred to cases he had described in which local epileptic attacks were similarly provoked by peripheral stimuli. During the investigation of the disturbances of sensation produced by cortical lesions he frequently found that the repeated or prolonged application of tactile or other stimuli excited local epileptic phenomena in the part stimulated, if a lesion existed in the proximity of the motor or sensory representation of this part in the cerebral cortex. These phenomena generally were clonic movements which usually spread in the manner of an ordinary Jacksonian attack, but occasionally they consisted of a numbness or tingling of the part stimulated, which often spread in the same way, or the part stimulated might become numb or "dead" and so anæsthetic that further investigation was impossible. One of his patients, a man with a gunshot wound in the region of the motor cortex of the left hemisphere, asserted that the continued use of his right hand, as in the employment of carpenter's tools, would bring on an epileptic attack starting in the hand.

He has also observed men with lesions in the neighbourhood of the visual cortex and subject to attacks of visual epilepsy, in whom epileptic visual phenomena were apparently brought on by a strong light stimulus, as a visit to a cinema. And he has seen patients with lesions, traumatic and neoplastic, in the neighbourhood of the auditory centre in whom epileptic attacks followed exposure to loud noises. All these cases are clearly parallel to that shown by Dr. Denny-Brown. On the other hand we have the converse in the well-known fact that a ligature around the limb, firm grasping of the convulsed part, or passive arrest of the spasms, may prevent the spread of a Jacksonian attack.

Dr. C. P. SYMONDS referred to one case in which epileptic attacks were easily excited by music, and especially by the sounds of brass instruments, and to a second patient subject to epileptic attacks commencing with spasms of his left toes in which description of an attack, or focusing of attention on its symptoms, would bring on a seizure.

Dr. R. IRONSIDE described the case of a patient in whom generalized epileptic seizures were provoked by music, and especially when he played the piano.

Dr. DENNY-BROWN, in reply, pointed out that as far as he is aware acustico-motor epilepsy is excited by unexpected sounds only. In the case he has presented the element of surprise is not a necessary factor. In his opinion it is impossible in the present state of our knowledge to determine the mechanisms concerned inthe production of an attack by peripheral stimuli.

Pituitary Tumour, with Goitre and Acromegaly.

By REDVERS IRONSIDE.

J. B., female, aged 60. Twenty-five years ago she began to take larger shoes and gloves and noticed a swelling appearing in the neck. Fifteen years ago, a retrosternal goitre was partially removed on account of breathlessness, with residual paralysis of the left recurrent laryngeal nerve. The patient has complained of headache, which has not been severe during the past year. No giddiness, faints or vomiting.

On examination.—Typical acromegalic appearance with hypertrophic changes in the interphalangeal and elbow joints. Hard swelling in the region of the thyroid. Fields of vision bi-temporally constricted to red and green, but not to white. Skiagram of sella turcica shows considerable enlargement. Shotty glands in both supraclavicular regions. Symmetrical enlargement of submaxillary glands. Hæmorrhages in both fundi. Blood-pressure, 220/165. Urine contained a trace of albumin, but no sugar.

Dr. P. CLOAKE referred to a similar case in which during life obstinate constipation was a prominent symptom, and after death there was found an enormous enlargement of the bowels. He raised the question as to whether a defect or disturbance of pituitary secretion was responsible for the fæcal stagnation. He described another case of acromegaly in which during the course of deep X-ray applications to the pituitary a goitre developed.

Spinal Caries with Compression Paraplegia.

By HUGH G. GARLAND.

T. B., male, aged 62. Admitted to hospital, July 17, 1929, complaining of pain encircling the trunk at the level of the umbilicus of eighteen months' duration. It is increased on coughing or sneezing. Six months ago weakness of the legs developed rapidly with incontinence of urine and fæces: three weeks later sphincter control returned and has been normal since. There has been numbness in both legs for two months and occasional flexor spasms. General health is very good. He had a urethral discharge at age of 25 (untreated).

Physical examination.—Some weakness of both legs with symmetrical muscular wasting and a mild degree of spasticity. Weakness of lower half of rectus abdominis. Hypalgesia over legs and lower trunk, with impairment of temperature and vibration sensibility over the same area. Upper border of sensory loss is at level of umbilicus. Gait slightly spastic. Knee-jerks exaggerated: bilateral knee and ankle clonus and extensor plantar responses.

Prominent veins over upper part of chest. Dullness to percussion in front at inner end of second left intercostal space and to right of eighth and ninth dorsal spines over an area about 4 in. in diameter, with diminished air entry over same area. Marked prominence of eighth dorsal spine and of ninth rib on each side. Second aortic sound accentuated. Blood-pressure 174/108 mm.

Second examination.—X-rays: ninth dorsal vertebra is evenly collapsed; intervertebral discs and the vertebral bodies above and below are normal. An opacity, roughly circular in outline and 4 in. diameter, extends to the right of the collapsed vertebra and shows central patchy calcification. There is bulging of the descending arch of the aorta and continuous with this below is the convex shadow of the descending aorta which is displaced or dilated. Old fracture of eighth and ninth left ribs.

Cerebrospinal fluid: Pressure 100 mm., with no rise on jugular compression. Slightly yellow fluid; 2 cells per c.mm.; protein, 0·18 per cent.; Lange curve, negative; Wassermann reaction, negative.

Blood: Wassermann reaction 4444. Sedimentation rate normal.

Tuberculin skin test negative.

After a course of novarsenobillon, mercury, bismuth and potassium iodide, the blood Wassermann reaction, the general condition, and the cerebrospinal fluid are unchanged.

The lesion is regarded as inflammatory rather than neoplastic. The fact that the lungs have not been invaded is in favour of this view. The escape of the intervertebral disc shows that the process is not tubercular.

Dr. A. FEILING suggested that the radiographic appearances were in favour of a chronic abscess, which possibly commenced in an osteomyelitis.

Dr. C. P. SYMONDS said that despite the clear-cut shadow seen in the skiagrams there could be, in his opinion, little doubt that the primary lesion was neoplastic, possibly a sarcoma which often runs a chronic course. The involvement of the ribs is also in favour of this. He thought, however, that the possibility of hydatic disease should be considered.

Dr. J. P. MARTIN considered that though the symptoms have not advanced during the last three months, a new growth was the most probable diagnosis. He agreed that though the blood Wassermann reaction is positive the lesion is not syphilitic, though he recalled that Gowers had described paravertebral syphilitic masses.

Polyneuritis Cranialis.

By REDVERS IRONSIDE.

W. R., aged 18, a car-boy. Admitted to Guy's Hospital, under Dr. Poulton, August 8, 1929, on account of gradually oncoming right ptosis, noticed a fortnight before. Patient had felt in his usual health and pulse and temperature had been normal. Within the past week he had noticed numbness over the right eye.

On examination.—A pale, spare youth, with complete right ptosis. Optic discs, visual acuity and fields of vision, normal. Right pupil larger than left, and reacts very sluggishly to light and on convergence. Left pupil normal. Complete external ophthalmoplegia, except for some power remaining in the left external rectus. Sensory loss to pin-prick and cotton wool over first division of right fifth. Complete palsy of the right side of the face, upper and

lower. Other cranial nerves normal. No deafness or otorrhœa. No sensory, motor or reflex abnormality. Urine normal. No glands palpable in neck. Spleen not enlarged.

Cerebrospinal fluid: eight cells per cubic millimetre; albumin, 0·04 per cent.; globulin positive: Wassermann reaction negative. Blood-pressure 110 mm.: Wassermann reaction negative.

This patient has never suffered from headaches or vomiting. Gradual recovery has been taking place. The pupils are now equal, central and circular and react to light directly and consensually, and on convergence. Slight weakness of both external recti remains. There is slight right ptosis and hyperæsthesia to cotton wool and pin-prick over the first division of the right fifth. Corneal reflexes brisk and equal. Slight right peripheral facial weakness. Other cranial nerves normal. No sensory, motor, or reflex abnormalities in the trunk or limbs. The case is presented for discussion and pathological diagnosis.

Lesion of Third, Fourth, Fifth and Sixth Left Cranial Nerves.

By LEWIS R. YEALLAND.

W. C., female, aged 27, in October, 1928, began to see double in artificial light. In February, 1929, diplopia became more or less constant and her left eyelid began to fall. In July the ptosis became complete and in addition she complained of stiffness and neuralgic pains in her left face and loss of the sense of taste and of smell on the left side. The symptoms have been gradually progressive except in January and June, when there was, on both occasions, definite improvement for about a fortnight.

Physical examination.—Optic discs and fields normal. Left eye presents ptosis, internal and external ophthalmoplegia and proptosis. When the eyes are at rest a small portion of sclera is visible between the left eye and its external canthus. On attempted conjugate deviation to the right, the left shows inhibition. Inability to deviate jaw to right; wasting of left temporal muscle and weakness of left masseter. Left corneal reflex absent; loss of sensation to pin-prick and heat and cold over all divisions of left trigeminal nerve. A sensation of a "small burn" is evoked on some contacts by pin-prick but not by thermal stimuli. Sense of taste lost throughout left side of tongue. On tests, the sensation of smell appears to be normal, although the patient is conscious of some defect. Examination of other cranial nerves showed no defect. Reflexes: right plantar is indefinite, otherwise the reflexes are normal. The blood, cerebrospinal fluid, blood-sugar and skiagram of skull showed nothing pathological.

Dr. R. IRONSIDE confessed he was mystified as to the nature of the lesion in his case. Unilateral symptoms, as those in Dr. Yealland's case, are often due to a tumour at the base of the brain, but the absence of headache argued against this diagnosis in this case. He suggested the nerves might be compressed by an aneurysm of the internal carotid artery.

Dr. W. J. ADIE agreed that an intracranial aneurysm was the most probable diagnosis in Dr. Yealland's case. He had recently seen similar symptoms in a patient who died shortly afterwards with apoplexy, the symptoms of which suggested rupture of an aneurysm.

Dr. WORSTER-DROUGHT did not think a tumour could be excluded. He described the case of a patient with the same signs in whom the ocular palsies had existed for seven years before headache appeared. The patient later developed papilloedema and at operation a large tumour was found in the middle fossa of the skull.

Dr. REES referred to a case recently in the Hospital under the care of Dr. Gordon Holmes. He developed gradually eleven years ago a complete internal and external ophthalmoplegia of the left eye, with pain and later anæsthesia in the distribution of the ophthalmic division of the trigeminal nerve. Ten years later his left eye became blind and slightly proptosed, and he began to suffer with slight headaches. Radiographs revealed a large partly calcified tumour, probably a psammoma, in the floor of the middle fossa of the skull. This case shows that headaches may be a late symptom in tumours of this region.

Sudden Paralysis in the Left Lower Limb, Associated with Hæmophilia.

By H. J. SEDDON.

S. L., male, aged 24, chauffeur.

History of present condition.—June 9, 1928: The patient was involved in a motor-car accident and admitted to Kingston Hospital. He was unconscious for three days as the result of "concussion." X-ray examination of spine showed fracture in region of third and fourth lumbar vertebræ; there was some injury to the right ankle, but apparently no bony lesion.

He remained on his back for four months, and returned to work six months after the accident—not wearing any form of spinal support. After the accident patient noticed that he occasionally lost control of his legs and fell. There was no paralysis and no loss of consciousness.

Early in 1929, he stumbled and injured right hip. A large swelling appeared in upper and outer part of thigh, but a skiagram did not show any fracture of femur and the swelling gradually disappeared.

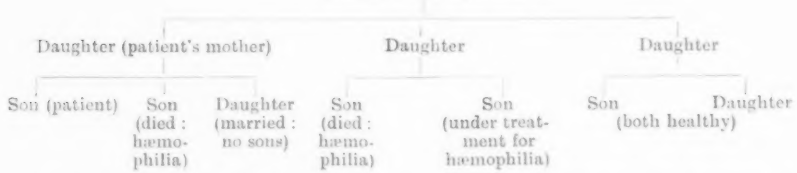
In May, 1929, his right ankle "gave way" and patient was admitted to hospital with a large swelling of that ankle, but again no fracture was found.

In June, 1929, after driving to Portsmouth without accident, became aware of sudden weakness in the left lower limb. The onset was instantaneous and he cannot recall feeling any pain. The paralysis has been substantially the same since.

September, 1929.—"Pins and needles" were sometimes felt in the right lower limb, but there was no muscular weakness of it.

Micturition is normal and the bowels are regular with medicine.

Family history.—The history of hæmophilia is summarized below :—



Past history.—In 1926 patient was admitted to hospital on account of severe hæmaturia and remained there for six months. There were no marked constitutional signs.

On examination.—Cranial nerves normal. In his left leg, the quadriceps extensor muscles are paralysed and no voluntary contraction can be detected in pectineus and adductor magnus. The adductor longus and tensor fasciæ femoris work well. No other muscular weakness found. Sensation: An area roughly corresponding to anterior division of L 3 and 4 in the left lower limb is insensitive to cotton wool, pin-prick and temperature. Vibration of tuning fork not felt on left patella, and only felt poorly at upper and lower ends of the fibula. General diminution in tactile sensibility in the whole of the left lower limb. Elsewhere no sensory changes can be found. Joint sensibility is everywhere normal. Reflexes: biceps, triceps, supinator and ankle-jerks strong and equal on both sides. Right knee-jerk easily obtained, left absent. The abdominal and cremasteric reflexes are normal. The plantar reflexes are flexor. Spine: movements are difficult to observe, but apparently normal. Skiagrams: the earlier skiagrams of spine are not now available: the recent ones show no abnormality of the spine.

Lumbar puncture has not been performed on account of the blood condition.

Dr. A. FEILING said that a local hæmatomyelia had to be considered, though he was not aware that this had been observed in hæmophilia. It appeared to him, however, more probable that the condition was due to compression of the roots by a large hæmorrhage into the psoas muscle.

Dr. J. P. MARTIN had never seen such symptoms produced by a hæmorrhage into the lumbosacral plexus. The absence of severe pain at the onset and the fact that little or no recovery had occurred, seemed to him in favour of a spinal lesion.

Dr. C. P. SYMONDS pointed out how closely the symptoms resemble those produced by a local hæmorrhage into the grey matter of the cord. He had no doubt this is the correct diagnosis in Mr. Seddon's case.

Dysarthria and Abnormal Gait.

By F. PARKES WEBER and O. B. BODE.

The patient, V. A., aged 25, is a strongly-built and well-developed man, who, when sitting at his ease, appears to be perfectly normal. His speech, however, is indistinct, and blurred or husky (not of the "scanning" dissemi-

nated sclerosis type), and when speaking he seems to be hampered by a spastic or hypertonic condition of the jaw-muscles. When he walks or when he stands upright (as if to attention) the upper part of his trunk is thrown rigidly back and slightly to the right, and, owing to very slight foot-drop, the left foot is raised somewhat more than the right. When he is speaking, the muscles of his neck and face tend to become spastic. He has a little dysphagia.

Spasm of the right orbicularis muscle seems to have been a prominent feature, but disappeared nearly twelve months ago. There is very slight lateral nystagmus to left. The tongue is protruded somewhat to the right. The patellar and Achilles reflexes are over-active on both sides. There is ankle clonus on the left side, but not definitely on the right. The plantar reflex on the right side is of the normal flexor type, whereas on the left side it either cannot be obtained or a Babinski phenomenon is "indicated." There is no inco-ordination. The maximum circumference of the left calf is 1 cm. less than that of the right calf; the circumference of the left thigh (20 cm. above the upper border of the patella) is $1\frac{1}{2}$ cm. less than that of the right thigh. There is a slight difference at times between the two halves of the face, which may be due to slight muscular hypotonicity on the right side or hypertonicity on the left side.

Nothing abnormal has been noted in the arms, nor in the superficial abdominal reflexes, the pupils, the ophthalmoscopic appearances or sensation. There are no tremors or abnormal choreic or rhythmical movements of any kind. No muscular bradykinesia. No greenish coloration at the corneal margins. Nothing abnormal in the liver, or spleen, or other abdominal or thoracic viscera; nor in the urine, excepting frequently slight excess of urobilinogen. The galactose test of hepatic function gives a negative result, and the blood-serum gives negative Wassermann and Meinicke reactions. The cerebrospinal fluid, when examined at another hospital, was normal and gave a negative Wassermann reaction. The patient seems to be of average intelligence, but perhaps almost abnormally cheerful (slight mental "euphoria"). Nothing abnormal in regard to emotional manifestations (crying, laughing, &c.) has been noted.

The patient is said to have two healthy brothers, and in the *family history* there is nothing abnormal excepting that his father developed right-sided hemiplegia at the age of 28 years, and died of pneumonia at the age of 53 years.

History.—Operation for appendicitis as a boy. Articular rheumatism at 16 years. Suppurative middle-ear disease and mastoid operation five years ago. The patient has always been fond of muscular exercise and can still stand on his hands with ease. In 1924 he had a job as labourer in London (using a sledge-hammer). When this job was over in 1925, he ran thirty-two miles in one day. On the following day he noticed that he was weak in the left foot, and that it tended to hang somewhat, and that in walking he had to raise it higher than the right foot; during the next two years he sometimes used a stick as a support. He thinks that the present illness commenced two

and a half years ago with muscular spasms about the right eye, and what he calls "gasping" movements of the mouth. He has had neither the orbicularis muscle spasms nor the "gasping" movements for nearly twelve months. The peculiar gait, dysarthria and slight dysphagia have developed during the last seven months. There is no history to suggest that he has had encephalitis of any kind.

In regard to *diagnosis* we have to consider some degenerative lesion affecting the motor tract, especially to the left leg, together with a superadded functional disturbance; or (2) the possibility of the whole syndrome being functional; or (3) an early and non-typical stage of chronic lenticular degeneration (Wilson's disease).

During demonstration of the case various members pointed out features that indicated a psychogenic rather than an organic origin of the symptoms. Dr. RIDDOCH said that not only does the tongue protrude strongly to the right but that in the mouth it is deviated into the right cheek, a condition not found in organic lingual palsy. Dr. GORDON HOLMES found the left plantar reflex normal, and as the left-sided ankle clonus persisted on strong plantar flexion of the great toe he did not regard it as a sign of organic disease.

Dr. R. D. GILLESPIE said that in his opinion the condition was hysterical: the mode of development of the symptoms was suspicious: no sign was present that could not be imitated; when the patient's attention was diverted the attitude of his trunk was normal, and finally the suggestion to the patient that he could control his symptoms was resented in the manner we commonly find in hysterical subjects.

A Case of Family Periodic Paralysis, with Attacks on Excitement.

By C. P. SYMONDS.

W. F., male, aged 28, locomotive fireman, has been subject to attacks of periodic paralysis since childhood. His younger brother and his mother are subject to similar attacks and the mother's father is said to have had the same complaint. The patient's attacks vary both in severity and duration; one, observed in hospital, lasted for an hour and a half and was of subacute onset. At its height all the voluntary muscles appeared to be affected, but none were completely paralysed. He was, however, quite helpless and inarticulate. All tendon-jerks were abolished. The plantar responses were flexor.

He states that although his attacks may come on without cause they are frequently occasioned by emotion. This may take the form of: (1) excitement, e.g., the cinema, or an exciting moment in a game: (2) fear, e.g., when he receives a summons to go before his superior officer; (3) fluster, e.g., if when doing a job he realizes suddenly that he cannot get it finished in time.

The case is presented as affording a possible link between family periodic paralysis and cataplexy.

Dr. L. R YEALLAND asked if the faradic excitability of the muscles was affected in the attacks. In a somewhat similar case he had seen he could

not, during an attack, produce contraction of the muscles by the faradic current.

Dr. J. P. MARTIN inquired if it were known that in family periodic paralysis excitement brought on attacks of loss of voluntary movement; he could not recall any statement that it did.

Dr. SYMONDS, in reply, said that there had been as yet no opportunity of testing the electrical responses of the muscles during an attack, and that he was not aware that excitement had been previously described as an exciting cause. It is noteworthy that in the patient presented the attacks are not brought on by fatigue, which is the rule in family periodic paralysis.

Arterial Angeioma of Brain.

By C. P. SYMONDS.

G. G., male, aged 44, carpenter, first seen in March, 1929, on account of epileptic attacks dating from the age of 15. The aura consisted of a "wheel of shining blue and silver lights," revolving in a counter-clockwise direction in the right half of the visual fields. As a rule this was followed in one or two minutes by a generalized convulsion. Occasionally a brief vision of "people running about" intervened between the aura of coloured lights and the convulsion. He had been conscious since boyhood of a noise in his head, which he compared to the puffing of a distant railway engine. Recently he had complained of severe headaches and failing vision, and had had an attack of numbness down the whole left side of his body.

On examination.—Showed marked dilatation of the vessels of the scalp, especially over the left parieto-occipital area. A musical bruit simultaneous with the carotid pulse was audible over the whole head, being loudest above and behind the left ear. A skiagram showed grooving of the inner table of the skull by a greatly enlarged and tortuous vessel whose maximal girth corresponds to the left occipital pole. The visual fields showed an incomplete right hemianopia. Early papilloedema was present on both sides. There was bilateral exophthalmos. Both carotid arteries appeared large, and the heart was enlarged 1 in. to the left (confirmed by skiagram).

On April 2, 1929, Mr. Bromley ligatured the left common carotid artery, and the patient has subsequently been subjected to deep X-ray therapy. He has had no fits since the operation. Headache is less and papilloedema has subsided. The bruit, though still audible above and behind the left ear, is less evident both to physician and patient.

Dr. PARKES WEBER pointed out that not only could the pulsations be heard by the patient, but they are audible to the observer if he inserts one end of a rubber tube into the patient's external auditory meatus and the other into his own ear.

Dr. GORDON HOLMES referred to the case of a man, aged 28, who commenced at the age of 16 to have epileptic attacks heralded by a ringing noise

in his right ear, and later by the sound of voices, associated with flashes of light in front of his eyes. In each attack he became unconscious quickly and had general convulsions.

Two years ago he began to suffer with headaches in the right temporal and frontal region, and found he could not see fully to his left. Lately the attacks have been preceded by a gustatory aura and a dreamy state. The superficial arteries of his scalp were dilated and pulsated strongly. Papilloedema was present, and the reflexes on his left side were exaggerated, but there was no disturbance of motor or sensory functions. He had a partial left-sided homonymous hemianopia. Sir Percy Sargent exposed the right temporal lobe and found it covered and infiltrated by dilated pulsating vessels. Three deep ligatures were inserted through the temporal lobe and later the right common carotid was ligatured. Since the operation he has had no epileptic seizures, but he still gets dreamy states associated by an unpleasant smell and a curious epigastric sensation. His visual fields have become full.

Pineal Syndrome (Ocular Palsies and Sexual Precocity) in a Boy, aged 10.

By W. J. Adie.

A. C., aged 12, complains of headache, double vision and shaking of the right arm. His health was very good until he began to have headaches about a year ago; six months later he began to see double and the right arm trembled when he used it. During the last three months he has had several generalized convulsions with unconsciousness. He was "very forward" mentally from the age of 5 years: at the age of 8 years he was "fully developed," and was not allowed to undress before his sisters. His parents are alive and well; he has five sisters and one brother aged 15, all healthy.

His sexual and general development is that of a well-grown youth of 18. Mentally he is intelligent but not precocious; his mother states that he has become dull during the last year. Speech is slow and slightly slurred. Smell, hearing and taste are normal. The optic discs are rather pale but the fields are full and vision is good when his myopia is corrected. When he first came under observation a month ago the pupils were equal and reacted briskly to light but poorly on convergence: upward movement of the eyeballs was absent; all other ocular movements were normal. Now the left pupil does not react to light and the right as it contracts becomes oval. Downward movement is defective in both eyes, but better right than left; lateral movements are good in the right eye, in the left inward, outward and convergent movements are defective. There is no ptosis or nystagmus. Apart from weakness of the left side of the face of lower neurone type, the other cranial nerves are normal.

Power in the right arm is good, but the limb is hypotonic and ataxic; a very coarse tremor, exactly like the intention tremor of disseminate sclerosis, occurs on voluntary movement. The right lower limb is also slightly hypotonic, but there is no tremor and his gait is normal: he

stands easily on the left leg alone but cannot do so on the right leg. The power, tone and co-ordination of the limbs on the left side are normal. All tendon jerks are slightly brisker right than left; the abdominal and plantar reflexes are normal. Sensation is normal for all forms except pin-prick, which is slightly diminished on the right limbs and trunk.

Radiological report: A very well developed head, rather like that of an adult. No calcification seen in pineal region. Ventriculograms show a considerable degree of internal hydrocephalus.

Dr. Adie said that the existence of a tumour had not yet been proved. Sir Percy Sargent had incised the brain and opened the right lateral ventricle at the junction of the posterior and descending horns; no tumour was seen or felt. He thought nevertheless that there was a tumour. The lesion was certainly progressive as the ocular palsies had increased under observation; there was certainly a lesion in the mid-brain; did the association of precocity with signs of a mid-brain lesion justify the diagnosis of pineal tumour?

Most cases of pineal tumour were seen in adults; in them there were no sexual changes, but he believed that a tumour of the pineal body in young male children usually, perhaps always, caused precocity. One case of precocity in a female child had been described.

Specimen of Pineal Tumour.

Shown by W. J. Adie.

The patient, a man aged 21, died a week after coming under observation. His father stated that the illness began four months ago with squint, headaches and vomiting; within a month he was almost blind and unable to stand. The patient said, "I feel all right, but the doctors think there is something wrong with me." He was unable to describe his symptoms and could not give much assistance in the physical examination.

Intense papillœdema was present in both eyes. Vision was reduced to counting fingers at 2 ft. The pupils were large and equal, they reacted slightly on convergence but not to light. Movement of the eyeballs upwards was defective, downwards good, outwards absent, on convergence poor. On looking to the left the right eye made slow, coarse, irregular nystagmoid movements; to the right the left eye made similar but finer and quicker movements. The corneal reflexes were brisk and equal. The jaw deviated to the left side when he opened his mouth. The left side of the face was weak. He was deaf in the left ear, a tuning fork on the vertex was referred to the right ear; the otologist reported he was a bad witness, but that tests suggest a partial lesion of the left eighth nerve. The remaining cranial nerves were normal.

His head was rotated to the right and inclined to the left. The limbs were very weak and flaccid; co-ordination, considering the degree of weakness, was not grossly affected. Sensation was normal. The tendon jerks were very brisk and equal on the two sides. The plantar responses were extensor. He

was unable to sit up or stand. He was incontinent of urine and fæces. His physical and sexual development were normal. Dr. Adie said there was no history of precocity in this case.

In view of the severe general symptoms, the character of the nystagmus and the signs of damage to the fifth, sixth, seventh and eighth nerves on the left side, he had expected to find a tumour in the left posterior fossa. He had not attached due importance to the inactive pupils and defective upward movement of the eyeballs in an advanced case like this; if one did not know the order in which the signs had appeared, it was difficult to decide which of them were of localizing value.

Dr. J. G. GREENFIELD described the pathological appearances in the brain. The tumour took origin from the pineal and extended backwards and laterally, infiltrating the tectum of the mid-brain, the posterior commissure and both optic thalami. Its structure was characteristic of a tumour of the pineal body. It contained clusters of large cells with rounded nuclei and one or two long fleshy processes which appeared to run considerable distances from the cell body, for bundles of such processes could be seen with no cell bodies or nuclei in them. The cell clusters or bundles of fibres were separated from each other by fairly wide zones of fibrous tissue in the meshes of which were many lymphocytes. The large cells and their processes had some of the characters of neuroglia cells, but no neuroglia fibrils could be demonstrated in them.

Notices of Recent Publications.

Handbuch der Neurologie des Ohres. Herausgegeben von G. Alexander, O. Marburg und H. Brunner. II Band. 2te Teil. S. 1228 mit 242 Abbildungen. Berlin und Wien: Urban und Schwarzenberg. 1929. Price 150 Marks.

This volume completes the comprehensive system of the "Neurology of the Ear" which has been issued in several parts by Viennese neurologists and aurists during the past four years. Several articles contained in it are of little immediate interest to neurologists, while some seem a little out of place in a textbook on the nervous disorders of the ear. This does not, however, detract from the value of the system, for the more points that can be made common ground to the neurologist and aurist will prove to be of benefit to both. Stern's long chapter of over 200 pages on the non-suppurative inflammatory lesions of the brain, including encephalitis lethargica, encephalitis, encephalitis associated with other infections, and disseminated sclerosis, for instance, scarcely establishes any relation to diseases of the ear, though it is an admirable monograph on these subjects. Bénesi and Sommer have written exhaustively on the toxic neuritis of the eight nerve, due to various exogenous poisons, or occurring in infections and metabolic diseases. Alexander contributes a series of chapters on the intracranial complications of aural infections, and Brunner deals with abscess of the temporal lobe in an article in which much interesting information on the differential diagnosis of this condition may be found. Syphilis of the eighth nerve and the aural complications of tabes and general paralysis are dealt with more concisely by Schacherl. The aural disturbances that may occur in association with increase of intracranial pressure are described by Fischer, who maintains that there may be a "Stauungsohr" similar in its origin to papillœdema.

To the neurologists the two most interesting chapters are that on disturbances of speech due to lesions of the temporal lobe by Bonvicini, and that on tumours of the temporal lobe by Marburg. The former includes an instructive historical review of the many theories of aphasia, including a very full résumé and a critical appreciation of the work of Head, as well as an objective presentation of the defects of speech produced by local lesions of the brain. Marburg's article is a very valuable contribution to the symptomatology and localization of tumours of the temporal lobe.

The Editors of this textbook must be congratulated on the completion of their enormous task, and deserve the gratitude of both neurologists and aurists for having provided a manual distinguished by the high level of the individual chapters and by the discrimination they have shown in the selection and arrangement of its subject matter.

Brain Mechanism and Intelligence. By K. S. Lashley. Pp. 186. Chicago: The University Press. 1929. Price 13s. 6d.

The experiments described by Lashley consist in the training of rats in a variety of motor habits, either before or subsequent to ablation of parts of the cerebral hemispheres, and in the employment of retention tests to ascertain the influence of the lesions so produced upon habits formed either prior to or after the injury.

Lashley finds that the capacity to form the habits tested (maze habit) is reduced by destruction of cerebral tissue in direct proportion to the quantity of tissue destroyed. Equal extent of destruction produces equal degree of retardation in learning, irrespective of the particular cyto-architectural fields involved in the lesion: that is to say, the capacity to learn a habit depends upon the amount of cortex available and not upon its localization or anatomical specialization.

The greater the complexity of the habit under examination, the greater is the retardation in its acquirement after cerebral ablations. Similarly, the capacity to retain a habit is affected in like manner by destruction of cerebral tissue.

From these observations Lashley concludes that the learning process and the retention of habits depend not upon any finely localized structural changes within the cortex, nor upon the laying down of specific functional pathways within it. On the contrary, the mechanism of integration appears to lie in the dynamic relations between the parts of the nervous system rather than upon details of structural differentiation.

In a preliminary chapter Lashley discusses the nature of intelligence, and the relation of the learning capcity to intelligence, and he gives reasons for supposing that the problems of cerebral function in higher animal forms do not differ essentially from those raised in the course of his experiments on rats.

La Syphilis Médullaire. Par Lortat-Jacob et Poumeau-Delille. Pp. 151. Paris: Masson et Cie. Price 14 francs.

Malaria Provoquée. Par Fribourg-Blanc. Pp. 120. Paris: Masson et Cie. Price 15 francs.

These two small volumes form part of a series published under the general title of "Médecine et Chirurgie Pratiques," a title which indicates their purpose and scope accurately. Both volumes have an exhaustive bibliography, but in both, as in so many French publications, a table of contents occupies the place of, and has to do duty for, an index.

Lortat-Jacob and Poumeau-Delille give a clear and comprehensive description of the various syndromes of spinal syphilis, tabes dorsalis not being included in their purview. They deal with their subject under the accepted headings of Ætiology, Pathogenesis, Morbid Anatomy, Symptomatology,

Diagnosis and Treatment. The chapters describing the various clinical pictures of spinal syphilis are admirably arranged and are clear and comprehensive, and by themselves would make the volume well worth careful study. In the chapter on Treatment, it is disappointing to find mercury relegated to a minor place, and its indications dismissed in a single line.

Fribourg-Blanc gives a brief historical account of the evolution of malarial therapy. His descriptions of the practical details of this mode of treatment, of its course and complications, of its indications and results are excellent, and he has produced a volume that may be unreservedly recommended.

Die Encephalitis lethargica : ihre Nachkrankheiten und ihre Behandlung. Von C. v. Economo. S. 251. Berlin und Wien: Urban und Schwarzenberg. 1929. Price 20 Marks.

Here we are presented by Economo, who first recognized and described the disease, with a clinical and pathological study of encephalitis lethargica based on his own experiences. The literature of the subject is not neglected, but his pages are happily not overburdened with references to articles that have added little to our knowledge or can claim recognition only on the grounds of priority. The history of the first outbreak of the disease in Vienna and of its spread over the world is particularly interesting, and so too is the critical study of earlier epidemics which may have been identical with or allied to it. The ætiology and epidemiology are fully discussed, and the symptoms of both its acute and chronic stages are described in considerable detail. The chapters on the pathological anatomy of encephalitis lethargica and of its sequels are excellent and concise, but more illustrations would have been useful to the student. As many other Continental authorities, the author emphasizes the value of intravenous injections of iodide combined with vaccineurin in the treatment of the acute stages, but he adds little to our ordinary therapy of the later complications of the disease. The final chapters on what encephalitis lethargica has taught us of the functions of the nervous system is particularly instructive and interesting.

Mental Deficiency. By A. F. Tredgold. Fifth edition. Pp. 535. London: Baillière, Tindall and Cox. 1929. Price 25s.

This book first appeared twenty-one years ago, and the four editions which have been published since then indicate how useful it has proved itself to be to students and practitioners. In the present edition numerous alterations have been made, some of them necessitated by recent legislation, and most of the chapters have been revised, but the original arrangement and classification is closely adhered to. The treatment and legal status of the mentally defective are carefully dealt with.

Principles of Experimental Psychology. By H. PIÉRON. Translated by J. B. Miner. Pp. 190. London: Kegan Paul, Trench, Trübner and Co. 1929. Price 10s. 6d.

This latest edition to the rapidly growing library of psychological textbooks is characterized by the lucid exposition of the author and his effort to apply, as far as possible, objective methods to the scientific study of mental functions. After two chapters, in which he deals with reactions and forms of behaviour, including instinctive reactions and sentiments, he discusses perceptions, the acquisition and elaboration of experience, the factors that determine mental efficiency, mental evolution and mental types. His treatment of the subject is developed on biological lines rather than on those of classical psychology, and the student consequently feels he is in closer contact with the subjects discussed than is the case in most textbooks. The translator has presented the book in readable and accurate English.

The Mott Memorial Volume. Contributions to Psychiatry, Neurology and Sociology. Pp. 401. London: H. K. Lewis. 1929. Price 21s.

The colleagues, friends and former pupils of the late Sir Frederick Mott have published in memory of him, in this handsome volume, a number of original papers, mainly on subjects in which Mott himself was particularly interested. The chief contributions to neurology are the articles by Winkler on the anatomical changes that follow removal of the cerebellum, that of Golla and Cook on an isometric study of the knee-jerk, Elliot Smith's contribution on variations in the folding of the visual cortex, and McCowan and Cook's study of the ocular symptoms of epidemic encephalitis. Most of the other contributions deal with psychiatric or sociological problems. Von Monakow has written a short history of Mott's life and a critical appreciation of the permanent value of his scientific work.

Die Blut-Liquorschranke. Eine physiologische und klinische Studie. Von P. Fr. K. WALTER. S. 223. Leipzig: Georg Thieme. 1929. Price 19 Marks.

That a monograph of this size can be written on the formation of the cerebrospinal fluid and what used to be called "meningeal permeability" is evidence of the great advances which have been made since Mestrezat published his first papers on the subject twenty years ago. To these advances the author has contributed with his bromide test, the value of which in the diagnosis of cerebral arteriosclerosis is now generally recognized. The book is not merely an apologia for this test, although the last half deals with little else, but is a fully documented account of all the work that has been done on the formation of the cerebrospinal fluid, and on what Lina Stern calls the "hæmato-encephalic barrier."

The first part of the book is devoted to the question whether the barrier between blood and cerebrospinal fluid acts as a Donnan membrane, or whether it possesses powers of selective filtration. Mestrezat was on the whole in favour of the former hypothesis, but Stern found definite evidence of selective action. Walter finds it difficult to accept the Donnan membrane theory as a complete explanation, but considers that all the factors acting on the blood side of the barrier (adsorption to proteins, rapid elimination, &c.) have not yet been fully examined. The value of his bromide permeability test depends on the answer to this question, for if bromide is treated differently from other salts it is not a satisfactory test for general plexus-meningeal permeability. He finds, however, that the results given by it are in accord with those of the older methods, and considers that the theoretical objections based on Stern's work are not sufficient to condemn the test, especially since there may be unexplained factors in her work which vitiate her results.

The bibliography given appears to be fairly complete as far as German literature is concerned but omits several of Mestrezat's early papers, and some important recent English and American references.

Le Liquide céphalo-rachidien. Par Dr. RIZER. Pp. 250 avec 24 figs Paris: Masson et Cie. 1929. Price 28 francs.

This book embodies the results of some years of intensive study of the cerebrospinal fluid and its pathways at the medical school of Toulouse. It is divided into four sections, of which the first, which deals chiefly with technique, and the last, which describes the commoner changes in the cerebrospinal fluid, are not of very special merit, although some valuable advice and information about meningococcal meningitis is to be found in the last section. The two middle sections, which deal respectively with the physiology of the fluid and with the various methods of locating tumours or obstructions by injections of gas, lipiodol or coloured solutions, are full of new and unfamiliar material. In the physiological section are to be found not only a full criticism of the American pioneer work on the subject, but also the results of many personal experiments on animals and observations on the human subject which corroborate and amplify this work. Riser was also able to corroborate many of the results of Stern's experiments on the hæmato-encephalic barrier, but disagrees with her interpretation of their meaning, taking what seems to us the only tenable view in the light of modern knowledge, that the power of selective filtration which the choroid plexus possesses is shared by all the capillaries of the central nervous system.

The section dealing with the localization of spinal and ventricular block by injection methods is also excellent. Each method is described in detail and its usefulness and disadvantages examined thoroughly. There are probably few neurologists who will not find something new and useful in this section.

Laboratory Guide to Vertebrate Dissection for Students of Anatomy. By A. B. Appleton. Cambridge University Press. 1929. Pp. 152. Price 6s.

In this book directions are given for the dissection of the lamprey, the dogfish, necturus, the green lizard and the dog. These animals are chosen as representing a rising scale in vertebrate evolution, and species such as the teleostean fishes, frogs and birds, which have become specialized away from the main trend of evolution have been purposely omitted. This book is intended for those who have already studied elementary biology or human anatomy, and to whom the simpler dissections are familiar. Consequently we find fairly elaborate descriptions of such structures as the eye, the internal ear and the brain, and although the author does not attempt to consider the anatomy of the central nervous system in detail, the comparison of the external appearance of the brains and skulls of the species described in this book would be a useful groundwork for neurology. The absence of illustrations was no doubt essential if the price was to be kept low, but it lessens the otherwise attractive appearance of the book.

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